

SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: R GITOMER Examiner # 369634 Date: 7/29/02
 Art-Unit: 1627 Phone Number 305-0732 Serial Number: 09/1695, 807
 Mail Box and Bldg/Room Location: 3019 Results Format Preferred (circle): PAPER DISK E-MAIL

If more than one search is submitted, please prioritize searches in order of need.

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: _____

Inventors (please provide full names): _____

Earliest Priority Filing Date: _____

For Sequence Searches Only Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.

Jan Delaval
 Reference Librarian
 Biotechnology & Chemical Library
 CM1 1807 - 703-308-4498
 jan.delaval@naps.gov

STAFF USE ONLY
 Searcher: an
 Searcher Phone #: 4498
 Searcher Location: 1627
 Date Searcher Picked Up: 5/15/02
 Date Completed: 5/15/02
 Searcher Prep & Review Time: 20
 Clerical Prep Time: 20
 Online Time: + 65

Type of Search	Vendors and cost where applicable
NA Sequence (#)	STN <input checked="" type="checkbox"/>
AA Sequence (#)	Dialog _____
Structure (#)	Questel/Orbit _____
Bibliographic	Dr.Link _____
Litigation	Lexis/Nexis _____
Fulltext	Sequence Systems _____
Patent Family	WWW/Internet _____
Other	Other (specify) _____

=> fil reg
FILE 'REGISTRY' ENTERED AT 15:30:06 ON 05 AUG 2002
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STRUCTURE FILE UPDATES: 4 AUG 2002 HIGHEST RN 442512-16-5
DICTIONARY FILE UPDATES: 4 AUG 2002 HIGHEST RN 442512-16-5

TSCA INFORMATION NOW CURRENT THROUGH January 7, 2002

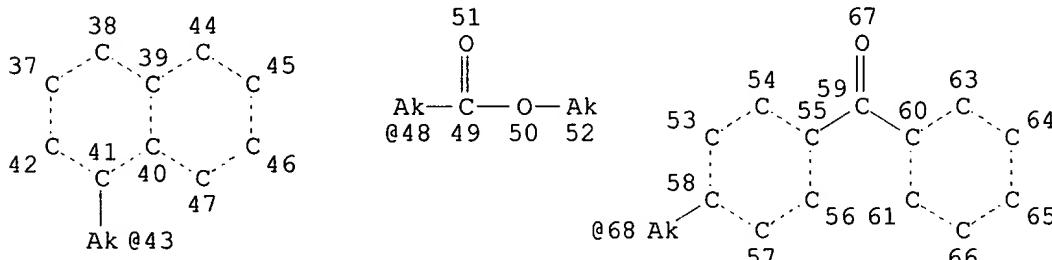
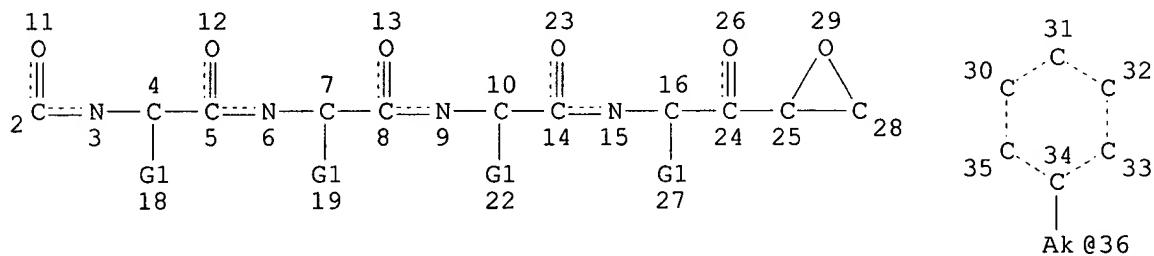
Please note that search-term pricing does apply when
conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Calculated physical property data is now available. See HELP PROPERTIES
for more information. See STNote 27, Searching Properties in the CAS
Registry File, for complete details:

<http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf>

=> d sta que 123
L20 STR



VAR G1=AK/36/43/48/68
NODE ATTRIBUTES:
CONNECT IS M1 RC AT 2
CONNECT IS M1 RC AT 25
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC 30 37 56 60
NUMBER OF NODES IS 63

STEREO ATTRIBUTES: NONE
L23 27 SEA FILE=REGISTRY SSS FUL L20

100.0% PROCESSED 1450 ITERATIONS
SEARCH TIME: 00.00.04

27 ANSWERS

=> d his

(FILE 'HOME' ENTERED AT 14:51:46 ON 05 AUG 2002)
 SET COST OFF

FILE 'REGISTRY' ENTERED AT 14:51:57 ON 05 AUG 2002

L1 1 S PROTEASOME/CN
 L2 1 S CHYMOTRYPSIN/CN
 L3 5 S 6493-05-6 OR 133343-34-7 OR 134381-21-8 OR 158442-41-2 OR 179
 L4 1 S NLVS/CN
 L5 3 S C28H43IN4O8S/MF AND 46.150.18/RID AND 1/NR
 L6 41 S C32H50N4O8/MF
 L7 13 S L6 AND 4/SQL
 L8 3 S C28H50N4O7/MF AND OC2/ES
 L9 2 S L8 NOT T/ELS
 L10 6 S C15H24N2O7S/MF AND NC4/ES
 L11 5 S L10 NOT GLYCINE
 L12 3 S L11 NOT T/ELS
 L13 1 S C19H25BN4O4/MF AND NC2NC2/ES
 L14 1 S L3 AND L7
 L15 2 S L5 NOT 125I
 L16 10 S L3, L4, L9, L12, L13, L14, L15
 L17 28 S C34H48N4O5/MF
 L18 2 S L17 AND OC2/ES
 L19 12 S L16, L18
 L20 STR
 L21 1 S L20 CSS
 L22 2 S L20
 L23 27 S L20 FUL
 SAV L23 GITOMER695/A
 L24 15 S L20 CSS FUL SUB=L23
 SAV L24 GITOMER695A/A
 L25 12 S L23 NOT L24
 L26 8 S L25 NOT (C5-C6-C6 OR NCNC2-SC4)/ES
 L27 6 S L26 NOT (T OR SI)/ELS
 L28 16 S L19, L27

FILE 'HCAPLUS' ENTERED AT 15:15:12 ON 05 AUG 2002

L29 2069 S L28
 L30 1598 S L29 AND (PY<=1998 OR PRY<=1998 OR AY<=1998)
 L31 73 S L30 AND L1
 L32 8 S L30 AND L2
 E BONE/CT
 E E3+ALL
 L33 72376 S E8+NT
 E E56+ALL
 L34 3731 S E4+NT
 L35 314 S E8+NT
 L36 2882 S E9+NT
 L37 2828 S E10+NT
 E BONE/CT
 E E3+ALL
 E E58+ALL
 L38 52158 S E3+NT
 E OSTEOPOROSIS/CT
 E E3+ALL
 L39 7181 S E6+NT
 E HYPERPARATHYROIDISM/CT
 E E3+ALL
 L40 1544 S E2
 L41 988 S METAST?(L)BONE(L)(DISEASE OR DISORDER)

L42 1026 S BONE, DISEASE/CT (L) FRACTURE
 L43 803 S BONE, NEOPLASM/CT (L) METAST?
 L44 141 S OSTEOLYT? (L) BONE (L) (DISEASE OR DISORDER)
 L45 2637 S BONE (L) (SURGERY OR SURGICAL OR POSTPLASTIC OR POST PLASTIC)
 L46 29 S L30 AND L33-L45
 L47 2 S L31, L32 AND L46
 L48 3 S PROSTH?/CW AND L30
 L49 1 S ISOPRENOID AND L30
 L50 4 S L47-L49
 L51 31 S L46, L50
 L52 2 S L30 AND (MUNDY G? OR GARRETT I? OR ROSSINI G?)/AU
 L53 2 S OSTEOSCREEN?/PA, CS AND L30
 L54 32 S L51-L53
 L55 30 S L54 AND (1 OR 63)/SC, SX
 L56 2 S L54 NOT L55
 L57 22 S L55 AND (BONE OR OSTE? OR JOINT OR CARTILAG? OR SKELET? OR H
 L58 18 S L55 AND (FRACTURE OR PROSTHE? OR ?NEOPLAS? OR ?TUMOR? OR ?MET
 L59 28 S L57, L58
 L60 2 S L55 NOT L59
 L61 1 S L60 NOT DEXAMETHASONE
 L62 29 S L59, L61
 L63 25 S L62 AND (1 OR 63)/SC
 L64 4 S L62 NOT L63
 SEL HIT RN L63

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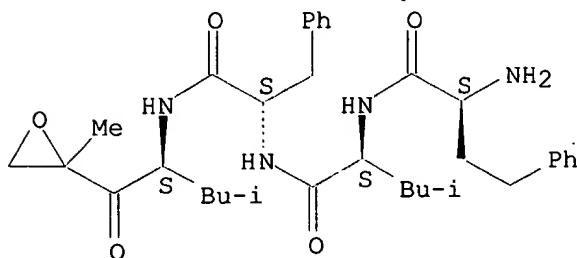
L65 4 S E1-E4
 L66 18 S L1, L2, L28, L65

FILE 'REGISTRY' ENTERED AT 15:30:06 ON 05 AUG 2002

=> d ide can tot 166

L66 ANSWER 1 OF 18 REGISTRY COPYRIGHT 2002 ACS
 RN 336099-21-9 REGISTRY
 CN L-Phenylalaninamide, (.alpha.S)-.alpha.-aminobenzenebutanoyl-L-leucyl-N-
 [(1S)-3-methyl-1-[(2-methyloxiranyl)carbonyl]butyl]- (9CI) (CA INDEX
 NAME)
 FS STEREOSEARCH
 MF C34 H48 N4 O5
 SR CA
 LC STN Files: CA, CAPLUS, TOXCENTER

Absolute stereochemistry.



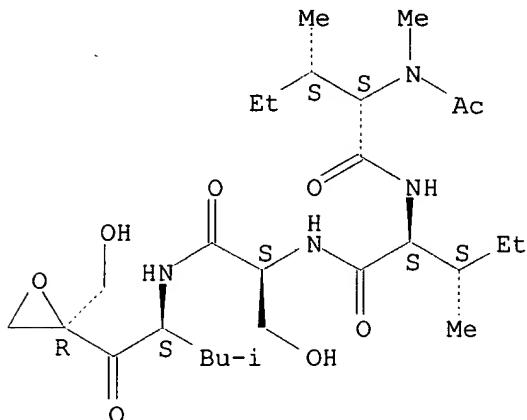
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
 1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:331618

L66 ANSWER 2 OF 18 REGISTRY COPYRIGHT 2002 ACS
 RN 259094-41-2 REGISTRY
 CN L-Serinamide, N-acetyl-N-methyl-L-isoleucyl-L-isoleucyl-N-[(1S)-1-[(2R)-2-(hydroxymethyl)oxiranyl]carbonyl]-3-methylbutyl] - (9CI) (CA INDEX NAME)
 FS PROTEIN SEQUENCE; STEREOSEARCH
 MF C27 H48 N4 O8
 SR CA
 LC STN Files: CA, CAPLUS, TOXCENTER

Absolute stereochemistry.

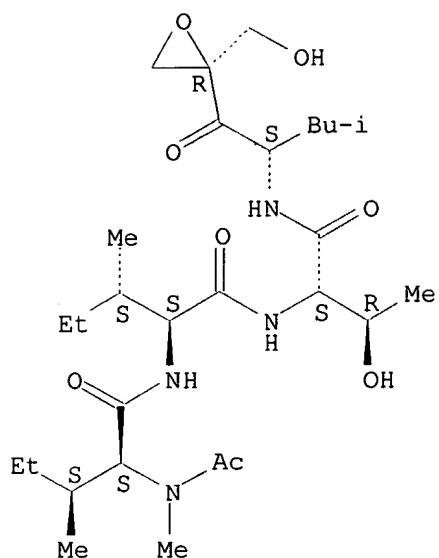


1 REFERENCES IN FILE CA (1967 TO DATE)
 1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 132:160826

L66 ANSWER 3 OF 18 REGISTRY COPYRIGHT 2002 ACS
 RN 259094-40-1 REGISTRY
 CN L-Threoninamide, N-acetyl-N-methyl-L-isoleucyl-L-isoleucyl-N-[(1S)-1-[(2R)-2-(hydroxymethyl)oxiranyl]carbonyl]-3-methylbutyl] - (9CI) (CA INDEX NAME)
 FS PROTEIN SEQUENCE; STEREOSEARCH
 MF C28 H50 N4 O8
 SR CA
 LC STN Files: CA, CAPLUS, TOXCENTER

Absolute stereochemistry.

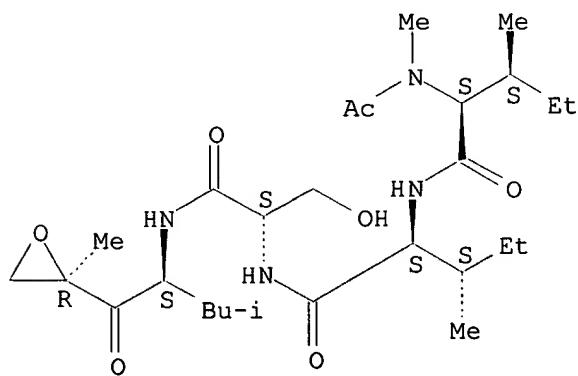


1 REFERENCES IN FILE CA (1967 TO DATE)
 1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 132:160826

L66 ANSWER 4 OF 18 REGISTRY COPYRIGHT 2002 ACS
 RN 259094-39-8 REGISTRY
 CN L-Serinamide, N-acetyl-N-methyl-L-isoleucyl-L-isoleucyl-N-[(1S)-3-methyl-1-[(2R)-2-methyloxiranyl]carbonylbutyl]- (9CI) (CA INDEX NAME)
 FS STEREOSEARCH
 MF C27 H48 N4 O7
 SR CA
 LC STN Files: CA, CAPLUS, TOXCENTER

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

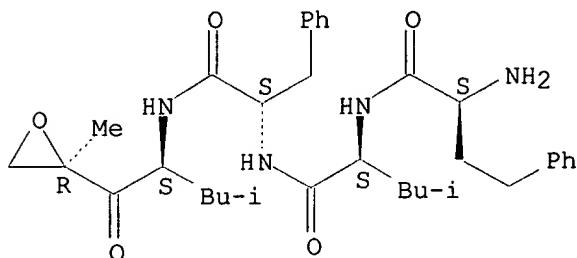
1 REFERENCES IN FILE CA (1967 TO DATE)
 1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 132:160826

L66 ANSWER 5 OF 18 REGISTRY COPYRIGHT 2002 ACS

RN 254888-44-3 REGISTRY
 CN L-Phenylalaninamide, (.alpha.S)-.alpha.-aminobenzenebutanoyl-L-leucyl-N-[(1S)-3-methyl-1-[(2R)-2-methyloxiranyl]carbonyl]butyl- (9CI) (CA INDEX NAME)
 FS STEREOSEARCH
 MF C34 H48 N4 O5
 SR CA
 LC STN Files: CA, CAPLUS

Absolute stereochemistry.



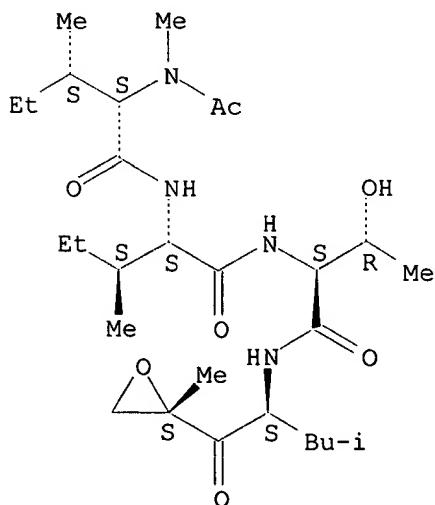
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
 1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 132:89911

L66 ANSWER 6 OF 18 REGISTRY COPYRIGHT 2002 ACS
 RN 247068-94-6 REGISTRY
 CN L-Threoninamide, N-acetyl-N-methyl-L-isoleucyl-L-isoleucyl-N-[(1S)-3-methyl-1-[(2S)-2-methyloxiranyl]carbonyl]butyl- (9CI) (CA INDEX NAME)
 FS STEREOSEARCH
 MF C28 H50 N4 O7
 SR CA
 LC STN Files: CA, CAPLUS, TOXCENTER

Absolute stereochemistry.



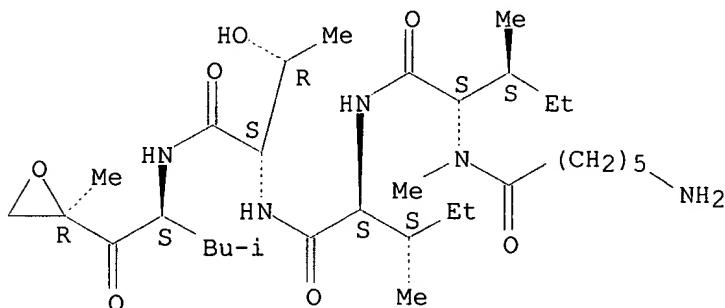
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
 1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 131:299679

L66 ANSWER 7 OF 18 REGISTRY COPYRIGHT 2002 ACS
 RN 247068-91-3 REGISTRY
 CN L-Threoninamide, N-(6-amino-1-oxohexyl)-N-methyl-L-isoleucyl-L-isoleucyl-N-[(1S)-3-methyl-1-[(2R)-2-methyloxiranyl]carbonyl]butyl- (9CI) (CA INDEX NAME)
 FS PROTEIN SEQUENCE; STEREOSEARCH
 MF C32 H59 N5 O7
 SR CA
 LC STN Files: CA, CAPLUS, TOXCENTER

Absolute stereochemistry.



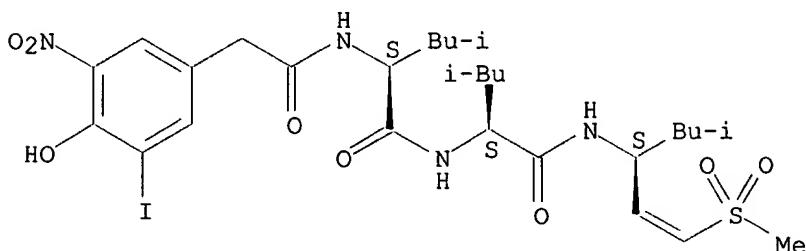
1 REFERENCES IN FILE CA (1967 TO DATE)
 1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 131:299679

L66 ANSWER 8 OF 18 REGISTRY COPYRIGHT 2002 ACS
 RN 211518-46-6 REGISTRY
 CN L-Leucinamide, N-[(4-hydroxy-3-iodo-5-nitrophenyl)acetyl]-L-leucyl-N-[(1S)-3-methyl-1-[2-(methylsulfonyl)ethenyl]butyl- (9CI) (CA INDEX NAME)
 FS STEREOSEARCH
 MF C28 H43 I N4 O8 S
 SR CA
 LC STN Files: CA, CAPLUS

Absolute stereochemistry.

Double bond geometry unknown.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)

1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 129:172314

L66 ANSWER 9 OF 18 REGISTRY COPYRIGHT 2002 ACS

RN 193482-49-4 REGISTRY

CN L-Leucinamide, N-[(4-hydroxy-3-iodo-5-nitrophenyl)acetyl]-L-leucyl-N-[(1S)-3-methyl-1-[(1E)-2-(methylsulfonyl)ethenyl]butyl]- (9CI) (CA INDEX NAME)

OTHER NAMES:

CN NLVS

FS STEREOSEARCH

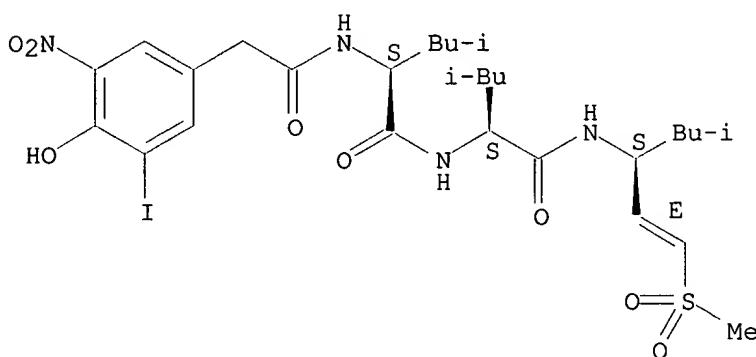
MF C28 H43 I N4 O8 S

SR CA

LC STN Files: CA, CAPLUS, TOXCENTER

Absolute stereochemistry.

Double bond geometry as shown.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

5 REFERENCES IN FILE CA (1967 TO DATE)

5 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 136:319354

REFERENCE 2: 135:193203

REFERENCE 3: 134:320576

REFERENCE 4: 134:278290

REFERENCE 5: 127:146407

L66 ANSWER 10 OF 18 REGISTRY COPYRIGHT 2002 ACS

RN 179324-69-7 REGISTRY

CN Boronic acid, [(1R)-3-methyl-1-[[[(2S)-1-oxo-3-phenyl-2-[(pyrazinylcarbonyl)amino]propyl]amino]butyl]- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Boronic acid, [3-methyl-1-[[1-oxo-3-phenyl-2-[(pyrazinylcarbonyl)amino]propyl]amino]butyl]-, [S-(R*,S*)]-

OTHER NAMES:

CN Bortezomib

CN LDP 341

CN MG 341

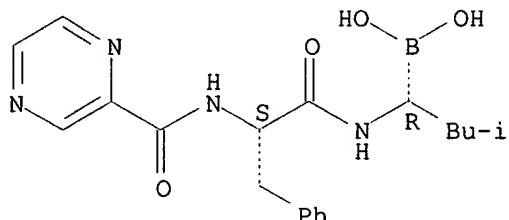
CN PS 341

CN PS 341 (pharmaceutical)

FS STEREOSEARCH

DR 197730-97-5
 MF C19 H25 B N4 O4
 SR CA
 LC STN Files: BIOSIS, BIOTECHNO, CA, CAPLUS, DRUGNL, DRUGUPDATES, EMBASE,
 PHAR, TOXCENTER, USPAT2, USPATFULL

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

40 REFERENCES IN FILE CA (1967 TO DATE)
 40 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 137:72751
 REFERENCE 2: 137:41335
 REFERENCE 3: 137:27901
 REFERENCE 4: 137:15379
 REFERENCE 5: 136:395418
 REFERENCE 6: 136:319393
 REFERENCE 7: 136:319354
 REFERENCE 8: 136:319018
 REFERENCE 9: 136:245552
 REFERENCE 10: 136:240926

L66 ANSWER 11 OF 18 REGISTRY COPYRIGHT 2002 ACS

RN 158442-41-2 REGISTRY

CN L-Alaninamide, N-[(phenylmethoxy)carbonyl]-L-isoleucyl-L-.alpha.-glutamyl-N-[(1S)-1-formyl-3-methylbutyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN L-Alaninamide, N-[(phenylmethoxy)carbonyl]-L-isoleucyl-L-.alpha.-glutamyl-N-[1-formyl-3-methylbutyl]-, 1,1-dimethylethyl ester, (S)-

OTHER NAMES:

CN 1: PN: WO0002548 PAGE: 29 claimed sequence

CN PSI

CN PSI (proteasome inhibitor)

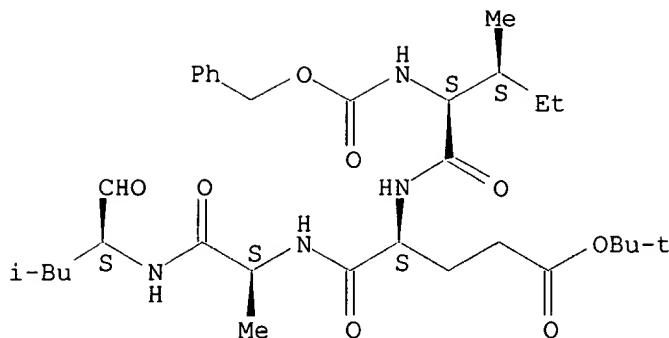
FS PROTEIN SEQUENCE; STEREOSEARCH

MF C32 H50 N4 O8

SR CA

LC STN Files: CA, CAPLUS, CHEMCATS, TOXCENTER, USPATFULL

Absolute stereochemistry.



28 REFERENCES IN FILE CA (1967 TO DATE)
 1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
 28 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 137:57227

REFERENCE 2: 137:41777

REFERENCE 3: 136:319354

REFERENCE 4: 136:290941

REFERENCE 5: 136:177564

REFERENCE 6: 136:90902

REFERENCE 7: 135:316891

REFERENCE 8: 135:271620

REFERENCE 9: 135:236171

REFERENCE 10: 135:205090

L66 ANSWER 12 OF 18 REGISTRY COPYRIGHT 2002 ACS

RN 154333-21-8 REGISTRY

CN L-Cysteine, N-acetyl-, 3-hydroxy-2-(1-hydroxy-2-methylpropyl)-4-methyl-5-oxo-2-pyrrolidinecarboxylate (ester), [2R-[2.alpha.,2(S*),3.beta.,4.beta.]]- (9CI) (CA INDEX NAME)

OTHER NAMES:

CN (6R,7S)-lactacystin

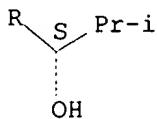
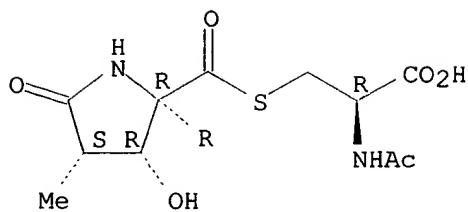
FS STEREOSEARCH

MF C15 H24 N2 O7 S

SR CA

LC STN Files: BIOTECHNO, CA, CAPLUS, EMBASE

Absolute stereochemistry. Rotation (+).



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

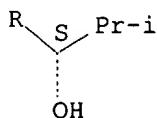
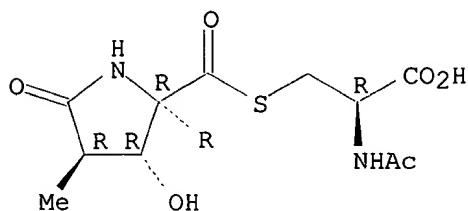
2 REFERENCES IN FILE CA (1967 TO DATE)
 2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 121:26250

REFERENCE 2: 120:245711

L66 ANSWER 13 OF 18 REGISTRY COPYRIGHT 2002 ACS
 RN 154006-00-5 REGISTRY
 CN L-Cysteine, N-acetyl-, 3-hydroxy-2-(1-hydroxy-2-methylpropyl)-4-methyl-5-oxo-2-pyrrolidinecarboxylate (ester), [2R-[2.alpha.,2(S*),3.beta.,4.alpha.]]- (9CI) (CA INDEX NAME)
 FS STEREOSEARCH
 MF C15 H24 N2 O7 S
 SR CA
 LC STN Files: CA, CAPLUS

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1967 TO DATE)
 2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 121:26250

REFERENCE 2: 120:218453

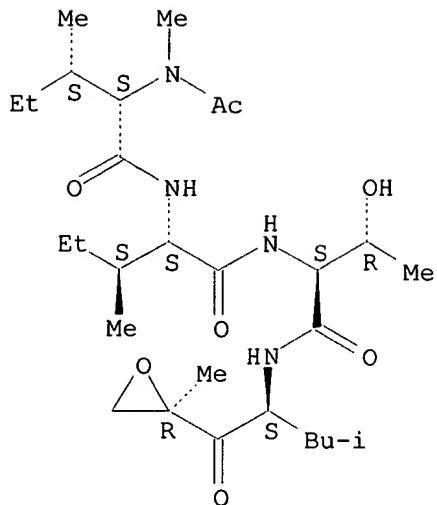
L66 ANSWER 14 OF 18 REGISTRY COPYRIGHT 2002 ACS
 RN 140879-24-9 REGISTRY
 CN Proteinase, multicatalytic (9CI) (CA INDEX NAME)
 OTHER NAMES:
 CN 26 S Protease
 CN Immunoproteasome
 CN Large multicatalytic protease
 CN Multicatalytic protease
 CN Multicatalytic proteinase
 CN Multicatalytic proteinase complex
 CN Organelle, proteasome
 CN Prosome
 CN **Proteasome**
 CN Tricorn protease
 CN Tricorn proteinase
 MF Unspecified
 CI MAN
 SR CA
 LC STN Files: ADISNEWS, AGRICOLA, BIOBUSINESS, BIOSIS, CA, CAPLUS, CEN, CIN, PIRA, PROMT, TOXCENTER, USPAT2, USPATFULL

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
 3264 REFERENCES IN FILE CA (1967 TO DATE)
 26 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
 3278 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 137:77649
 REFERENCE 2: 137:77156
 REFERENCE 3: 137:76832
 REFERENCE 4: 137:76498
 REFERENCE 5: 137:76300
 REFERENCE 6: 137:74641
 REFERENCE 7: 137:74352
 REFERENCE 8: 137:73225
 REFERENCE 9: 137:73223
 REFERENCE 10: 137:72751

L66 ANSWER 15 OF 18 REGISTRY COPYRIGHT 2002 ACS
 RN 134381-21-8 REGISTRY
 CN L-Threoninamide, N-acetyl-N-methyl-L-isoleucyl-L-isoleucyl-N-[(1S)-3-methyl-1-[(2R)-2-methyloxiranyl]carbonyl]butyl]-(9CI) (CA INDEX NAME)
 OTHER NAMES:
 CN BU 4061T
 CN Epoxomicin
 FS STEREOSEARCH
 MF C28 H50 N4 O7
 SR CA
 LC STN Files: AGRICOLA, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CEN, CHEMCATS, CSCHEM, EMBASE, MEDLINE, SYNTHLINE, TOXCENTER, USPATFULL

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

15 REFERENCES IN FILE CA (1967 TO DATE)
16 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE	1:	136:319354
REFERENCE	2:	136:210571
REFERENCE	3:	136:196058
REFERENCE	4:	135:254547
REFERENCE	5:	135:42638
REFERENCE	6:	134:331618
REFERENCE	7:	134:128358
REFERENCE	8:	133:148873
REFERENCE	9:	132:216387
REFERENCE	10:	132:160826

L66 ANSWER 16 OF 18 REGISTRY COPYRIGHT 2002 ACS

BN 133343-34-7 REGISTRY

RN 133343-34-7 REGISTRY
CN L-Cysteine, N-acetyl-, (2R,3S,4R)-3-hydroxy-2-[(1S)-1-hydroxy-2-methylpropyl]-4-methyl-5-oxo-2-pyrrolidinecarboxylate (ester) (9CI) (CA INDEX NAME)

INDEX NAMES;
OTHER CA INDEX NAMES:

CN L-Cysteine, N-acetyl-, 3-hydroxy-2-(1-hydroxy-2-methylpropyl)-4-methyl-5'-oxo-2-pyrrolidinecarboxylate (ester), [2R-[2.alpha.,2(S*),3.alpha.,4.alpha.,1]-

OTHER NAMES:

OTHER NAMES:

CN (1) Lactacy
CN Lactacystin

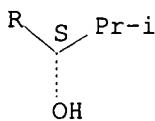
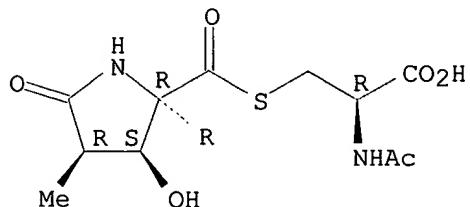
CN Lactacysein
ES STEREOSEARCH

CI COM

SR CA

LC STN Files: AGRICOLA, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CASREACT, CEN, CHEMCATS, CHEMINFORMRX, CSCHEM, EMBASE, MEDLINE, PHAR, PROMT, SYNTHLINE, TOXCENTER, USPAT2, USPATFULL

Absolute stereochemistry. Rotation (+).



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

186 REFERENCES IN FILE CA (1967 TO DATE)

14 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

187 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 137:3552

REFERENCE 2: 136:395463

REFERENCE 3: 136:363352

REFERENCE 4: 136:319393

REFERENCE 5: 136:319354

REFERENCE 6: 136:303940

REFERENCE 7: 136:226383

REFERENCE 8: 136:212412

REFERENCE 9: 136:210571

REFERENCE 10: 136:196263

L66 ANSWER 17 OF 18 REGISTRY COPYRIGHT 2002 ACS

RN 9004-07-3 REGISTRY

CN Chymotrypsin (9CI) (CA INDEX NAME)

OTHER NAMES:

CN .alpha.-Chymotrypsin

CN .alpha.-Chymotrypsin A

CN .alpha.1-Chymotrypsin

CN .gamma.-Chymotrypsin A

CN Alpha chymar

CN Alpha-chymar ophth

CN Avazyme
 CN Chymar
 CN Chymotest
 CN Chymotrypsin A
 CN Chymotrypsin A.alpha.
 CN Chymotrypsin B
 CN Chymotrypsin P
 CN E.C. 3.4.21.1
 CN E.C. 3.4.4.5
 CN E.C. 3.4.4.6
 CN Enzeon
 CN Quimar
 CN Quimotrase
 DR 8049-46-5, 9025-29-0, 9062-30-0, 9067-81-6
 MF Unspecified
 CI COM, MAN
 LC STN Files: AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMINFORMRX, CHEMLIST, CIN, CSCHEM, CSNB, DDFU, DIOGENES, DRUGU, EMBASE, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, NAPRALERT, NIOSHTIC, PHARMASEARCH, PIRA, PROMT, RTECS*, TOXCENTER, USAN, USPAT2, USPATFULL, VTB
 (*File contains numerically searchable property data)
 Other Sources: EINECS**, TSCA**, WHO
 (**Enter CHEMLIST File for up-to-date regulatory information)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
 10536 REFERENCES IN FILE CA (1967 TO DATE)
 657 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
 10549 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 137:83635
 REFERENCE 2: 137:79394
 REFERENCE 3: 137:79212
 REFERENCE 4: 137:78787
 REFERENCE 5: 137:75558
 REFERENCE 6: 137:75409
 REFERENCE 7: 137:75219
 REFERENCE 8: 137:73248
 REFERENCE 9: 137:62641
 REFERENCE 10: 137:62258

L66 ANSWER 18 OF 18 REGISTRY COPYRIGHT 2002 ACS
 RN 6493-05-6 REGISTRY
 CN 1H-Purine-2,6-dione, 3,7-dihydro-3,7-dimethyl-1-(5-oxohexyl)- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Theobromine, 1-(5-oxohexyl)- (7CI, 8CI)

OTHER NAMES:

CN 1-(5-Oxohexyl)-3,7-dimethylxanthine

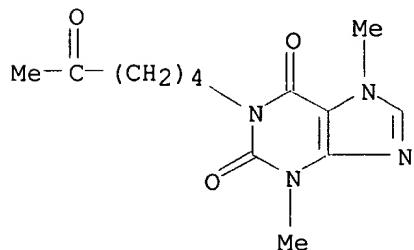
CN 1-(5-Oxohexyl)theobromine

CN 3,7-Dihydro-3,7-dimethyl-1-(5-oxohexyl)-1H-purine-2,6-dione

CN 3,7-Dimethyl-1-(5-oxohexyl)-1H,3H-purin-2,6-dione

CN 3,7-Dimethyl-1-(5-oxohexyl)xanthine

CN Agapúrin Retard
CN BL 191
CN Dimethyloxohexylxanthine
CN Oxpentifylline
CN Pentoxyfillin
CN Pentoxyfilline
CN Pentoxyphyllin
CN Pentoxyphylline
CN Pentoxyfilline
CN Pentoxyphyllin
CN PTX
CN Torental
CN Trental
FS 3D CONCORD
MF C13 H18 N4 O3
CI COM
LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*,
BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAOLD, CAPLUS,
CASREACT, CBNB, CEN, CHEMCATS, CHEMLIST, CIN, CSCHEM, DDFU, DIOGENES,
DRUGNL, DRUGPAT, DRUGU, DRUGUPDATES, EMBASE, IPA, MEDLINE, MRCK*,
NIOSHTIC, PHAR, PHARMASEARCH, PROMT, RTECS*, SPECINFO, SYNTHLINE,
TOXCENTER, USAN, USPAT2, USPATFULL, VETU
(*File contains numerically searchable property data)
Other Sources: EINECS**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1816 REFERENCES IN FILE CA (1967 TO DATE)
22 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
1821 REFERENCES IN FILE CAPLUS (1967 TO DATE)
2 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE	1:	137:83755
REFERENCE	2:	137:83612
REFERENCE	3:	137:72854
REFERENCE	4:	137:57306
REFERENCE	5:	137:57274
REFERENCE	6:	137:57200
REFERENCE	7:	137:56985
REFERENCE	8:	137:41772
REFERENCE	9:	137:41462

REFERENCE 10: 137:41310

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=> fil hcaplus
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FILE LAST UPDATED: 4 Aug 2002 (20020804/ED)

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=> d all hitstr tot 163

L63 ANSWER 1 OF 25 HCAPLUS COPYRIGHT 2002 ACS
AN 2002:483066 HCAPLUS
DN 137:41777
TI Inhibitors of NF-.kappa.B or proteasomal activity for stimulating hair growth
IN Mundy, Gregory R.; Garrett, I. Ross; Rossini, G.
PA Osteoscreen, Inc., USA
SO U.S., 9 pp., Cont.-in-part of U. S. Ser. No. 113,947.
CODEN: USXXAM
DT Patent
LA English
IC ICM A61K038-00
NCL 514012000
CC 1-12 (Pharmacology)
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6410512	B1	20020625	US 1999-361775	19990727 <--
	US 2002103127	A1	20020801	US 2002-50425	20020115 <--
PRAI	US 1998-113947	A2	19980710 <--		
	US 1999-361775	A1	19990727		
AB	Compds. that inhibit the activity of NF-.kappa.B or inhibit the activity of the proteasome or both promote hair growth and stimulate the prodn. of hair follicles and are thus useful in stimulating hair growth, including hair d., in subjects where this is desirable.				
ST	proteasome inhibitor hair growth stimulation; NFkappaB inhibitor hair growth stimulation				
IT	Human				

(NF-.kappa.B inhibitor or proteasomal activity inhibitor for stimulating hair growth)

IT Leukemia inhibitory factor
 Platelet-derived growth factors
 Transforming growth factors
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (NF-.kappa.B inhibitor or proteasomal activity inhibitor for stimulating hair growth, and use with other agents)

IT Chemotherapy
 (alopecia from; NF-.kappa.B inhibitor or proteasomal activity inhibitor for stimulating hair growth)

IT Temperature
 (cold, protection from; NF-.kappa.B inhibitor or proteasomal activity inhibitor for stimulating hair growth)

IT Hair
 (follicle; NF-.kappa.B inhibitor or proteasomal activity inhibitor for stimulating hair growth)

IT Alopecia
 (from chemotherapy; NF-.kappa.B inhibitor or proteasomal activity inhibitor for stimulating hair growth)

IT Disease, animal
 (genetic; NF-.kappa.B inhibitor or proteasomal activity inhibitor for stimulating hair growth)

IT Skin
 (growth or infiltration, agents promoting; NF-.kappa.B inhibitor or proteasomal activity inhibitor for stimulating hair growth, and use with other agents)

IT Hair preparations
 (growth stimulants; NF-.kappa.B inhibitor or proteasomal activity inhibitor for stimulating hair growth)

IT Aging, animal
 (hair thinning from; NF-.kappa.B inhibitor or proteasomal activity inhibitor for stimulating hair growth)

IT Alopecia
 (male pattern; NF-.kappa.B inhibitor or proteasomal activity inhibitor for stimulating hair growth)

IT Hair
 (thinning, aging-related; NF-.kappa.B inhibitor or proteasomal activity inhibitor for stimulating hair growth)

IT **158442-41-2**
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (NF-.kappa.B inhibitor or proteasomal activity inhibitor for stimulating hair growth)

IT 9002-64-6, Parathyroid hormone 61912-98-9, Insulin-like growth factor 62031-54-3, Fibroblast growth factor 62229-50-9, Epidermal growth factor
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (NF-.kappa.B inhibitor or proteasomal activity inhibitor for stimulating hair growth, and use with other agents)

IT 438573-00-3 438573-01-4
 RL: PRP (Properties)
 (unclaimed sequence; inhibitors of NF-.kappa.B or proteasomal activity for stimulating hair growth)

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

(1) Anon; WO 9718239 1997 HCPLUS
 (2) Anon; WO 9943346 1999 HCPLUS
 (3) Fenteany; US 6147223 A 2000 HCPLUS

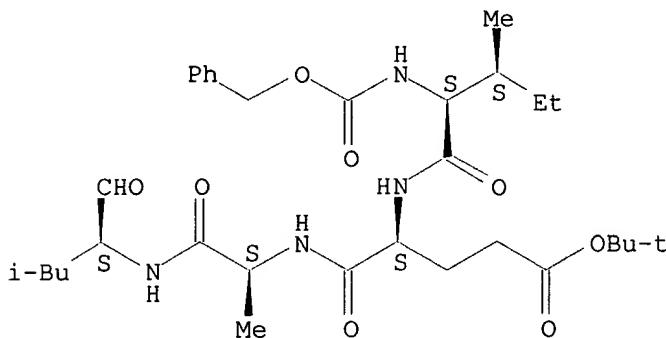
IT **158442-41-2**
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(NF-.kappa.B inhibitor or proteasomal activity inhibitor for stimulating hair growth)

RN 158442-41-2 HCPLUS

CN L-Alaninamide, N-[(phenylmethoxy)carbonyl]-L-isoleucyl-L-.alpha.-glutamyl-N-[(1S)-1-formyl-3-methylbutyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L63 ANSWER 2 OF 25 HCPLUS COPYRIGHT 2002 ACS

AN 2001:703740 HCPLUS

DN 135:251986

TI Methods for treating fibroproliferative diseases with antiproliferative or antifibrotic agents, especially antisense c-Jun oligonucleotides

IN Peterson, Theresa C.

PA Dalhousie University, Can.

SO U.S., 13 pp., Cont.-in-part of U.S. 6,025,151.

CODEN: USXXAM

DT Patent

LA English

IC ICM C12Q001-02

ICS C12Q001-00; C12Q001-50

NCL 435029000

CC 1-12 (Pharmacology)

Section cross-reference(s): 9, 63

FAN.CNT 4

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6294350	B1	20010925	US 1999-433621	19991102 <--
	US 5985592	A	19991116	US 1997-870096	19970605 <--
	US 6025151	A	20000215	US 1998-92317	19980605 <--
	WO 2001032156	A2	20010510	WO 2000-IB1731	20001102
				W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM	
				RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG	

PRAI US 1997-870096 A2 19970605 <--
 US 1998-92317 A2 19980605 <--
 US 1999-433621 A1 19991102

AB In accordance with the present invention, fibroproliferative disease or condition characterized by such symptoms as increased levels of c-Jun homodimers, increased heterodimerization of c-Jun with another signaling peptide, increased levels of phosphorylated c-Jun, or increased presence

of Jun kinase are treated by administering to the subject an amt. of a compd. effective to ameliorate one or more of the symptoms of the disease or condition, for example, an antiproliferative or antifibrotic agent. Preferred compds. for administration according to the invention are antisense c-Jun oligonucleotides and compds. that block c-Jun phosphorylation, such as pentoxifylline, or a functional deriv. or metabolite thereof. Also provided by the present invention are in vitro tests for identifying whether a test compd. is useful for treatment of a subject afflicted with such a disease and kits useful for conducting such assays.

ST fibroproliferative disease treatment antiproliferative antifibrotic agent; antiproliferative antisense oligonucleotide fibroproliferative disease cJun

IT Peptides, biological studies
 RL: ADV (Adverse effect, including toxicity); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
 (ATF2; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

IT Angiotensin receptors
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (AT1, inhibitors; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

IT Hepatitis
 (C; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

IT Transcription factors
 RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
 (CREB (cAMP-responsive element-binding); antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

IT Eye, disease
 Graves' disease
 (Graves' ophthalmopathy; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

IT Sarcoma
 (Kaposi's; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

IT Neoplasm
 (Li-Fraumeni syndrome; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

IT Transcription factors
 RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); OCCU (Occurrence)
 (NF-.kappa.B (nuclear factor .kappa.B); antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

IT Peptides, biological studies
 RL: ADV (Adverse effect, including toxicity); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
 (Nrf1; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

IT Eye
 (Tenon's capsule, fibroproliferation; antiproliferative or antifibrotic

agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

IT **Leukemia**
(acute myelogenous; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

IT **Abdomen**
(adhesions; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

IT **Fibrosis**
(antifibrotics; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

IT **Alzheimer's disease**
Animal tissue culture
Anti-Alzheimer's agents
Antitumor agents
Drug screening
Epithelium
Fibroblast
Hematopoietic precursor cell
Keloid
Kidney, disease
Leprosy
Mesenchyme
Multiple sclerosis
Myelodysplastic syndromes
Myeloproliferative disorders
Neoplasm
Neuroglia
Phosphorylation, biological
Picrorhiza kurroa
Signal transduction, biological
Silicosis
Silybum marianum
Test kits
(antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

IT **Platelet-derived growth factors**
Tumor necrosis factors
RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); OCCU (Occurrence)
(antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

IT **Antisense oligonucleotides**
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

IT **Decorins**
Phosphatidylcholines, biological studies
Tocopherols
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

IT **Bronchi**
(bronchiolitis, obliterative; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

IT Signal peptides
RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(c-Jun heterodimerization with; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

IT Transcription factors
RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BPN (Biosynthetic preparation); BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); OCCU (Occurrence); PREP (Preparation); PROC (Process)
(c-jun; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

IT Malaria
(cerebral; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

IT Intestine, disease
(colitis, collagenous; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

IT Cardiovascular system
(disease; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

IT Drugs
Ergot (Claviceps)
(drug-induced ergotism; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

IT Reproductive tract
(female, **cancer**; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

IT Intestine
Lung
Skin
(fibroblasts of; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

IT Radiation
(fibrosis from; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

IT Heart, disease
Kidney, disease
Liver, disease
Lung, disease
Peritoneum
(fibrosis; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

IT Gene, animal
RL: BPN (Biosynthetic preparation); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PREP (Preparation); PROC (Process)
(for c-Jun; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

IT Neuroglia
(glioblastoma, sporadic; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

IT Neuroglia
(glioblastoma; antiproliferative or antifibrotic agents, esp. antisense

IT c-Jun oligonucleotides, for treating fibroproliferative diseases)

IT Kidney, disease
(glomerulonephritis; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

IT Neutrophil
(infiltration; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

IT Intestine, disease
(inflammatory; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

IT Cytokines
RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); OCCU (Occurrence) (inflammatory; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

IT Drug delivery systems
(inhalants; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

IT Drug delivery systems
(injections, i.m.; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

IT Drug delivery systems
(injections, i.v.; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

IT Lung, disease
(interstitial; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

IT Brain, disease
(malaria; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

IT **Antitumor** agents
(mammary gland; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

IT Kidney
(mesangium; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

IT Leukemia
(myelogenous; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

IT Liver
(myofibroblasts of; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

IT Mammary gland
(neoplasm, inhibitors; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

IT Mammary gland
(neoplasm; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

IT Nerve, **neoplasm**
(neuroblastoma; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

IT Drug delivery systems
(oral; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

IT Proteins, specific or class
RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); OCCU (Occurrence)
(p65, NF-.kappa.B p65; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

IT Phosphatidylcholines, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(polyenyl-; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

IT Proliferation inhibition
(proliferation inhibitors; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

IT Disease, animal
(proliferative; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

IT Drug delivery systems
(rectal; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

IT Connective tissue
(scleroderma; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

IT Shock (circulatory collapse)
(septic; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

IT Blood vessel
(smooth muscle; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

IT Muscle
(smooth; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

IT Carcinoma
(squamous cell, differentiation disorder; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

IT Cell differentiation
(squamous cell, disorder; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

IT Drug delivery systems
(sustained-release; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

IT Lupus erythematosus
(systemic, nephritis assocd. with; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

IT Drug delivery systems
(topical; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

IT Drug delivery systems
(transdermal; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

IT Interferons
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(.alpha.; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)
 IT Transforming growth factors
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (.beta.-, RII/FC; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)
 IT 155215-87-5, Jun kinase
 RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); OCCU (Occurrence) (antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)
 IT 217308-10-6, DNA, d(G-C-A-G-T-C-A-T-A-G-A-A-C-A-G-T-C-C-G-T-C-A-C-T-T-C-A-C-G-T)
 RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
 (antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)
 IT 50-23-7, Hydrocortisone 54-85-3, Isoniazid 54-85-3D, Isoniazid, conjugated 59-67-6, Niacin, biological studies 64-86-8, Colchicine 107-35-7, Taurine 518-34-3, Tetrandrine 1028-33-7, Pentifylline 1405-86-3, Glycyrrhizin 6493-05-6, Pentoxifylline 6493-05-6D, Pentoxifylline, derivs. and metabolites 6493-06-7, 1H-Purine-2,6-dione, 3,7-dihydro-1-(5-hydroxyhexyl)-3,7-dimethyl-10102-43-9, Nitric oxide, biological studies 53179-13-8, Pirfenidone 55242-55-2, Propentofylline 55837-20-2, Halofuginone 62571-86-2, Captopril 75847-73-3, Enalapril 80288-49-9, Furafylline 83150-76-9, Octreotide 85721-33-1, Ciprofloxacin 91161-71-6, Terbinafine 114798-26-4, Losartan 119290-87-8, Acanthoic acid 120210-48-2, Tenidap RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)
 IT 50-88-4, Tritiated thymidine, biological studies 1148-63-6, Thymidine-.alpha.-t 42459-79-0, Uridine, 5-bromo-, labeled with tritium RL: BPR (Biological process); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
 (antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)
 IT 330196-64-0, Cytochrome p 450 1A2
 RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
 (inhibitors; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)
 IT 9015-82-1, Angiotensin converting enzyme
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (inhibitors; antiproliferative or antifibrotic agents, esp. antisense c-Jun oligonucleotides, for treating fibroproliferative diseases)

RE.CNT 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD

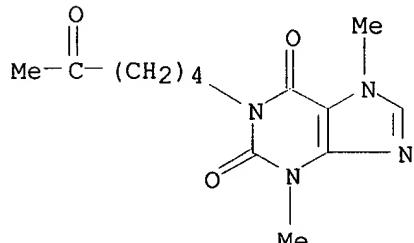
RE

- (1) Anon; DE 3604149 A1 1987 HCAPLUS
- (2) Anon; WO 8700523 A2 1987 HCAPLUS
- (3) Anon; WO 9219772 A1 1992 HCAPLUS
- (4) Anon; EP 0544391 A1 1993 HCAPLUS
- (5) Anon; WO 9502051 A2 1995 HCAPLUS

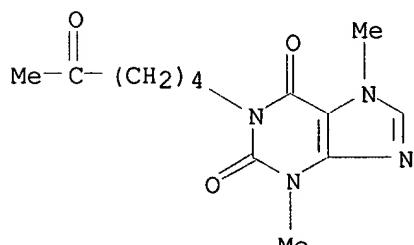
(6) Anon; WO 9526727 A1 1995 HCAPLUS
 (7) Bamberger; Proc Natl Acad Sci USA 1996, V93, P6169 HCAPLUS
 (8) Bessler; J Leukocyte Biol 1986, V40, P747 HCAPLUS
 (9) Bianco; US 5585380 1996 HCAPLUS
 (10) Bonsen; US 4265874 1981 HCAPLUS
 (11) Peterson; US 5985592 1999 HCAPLUS
 (12) Peterson; US 6025154 2000 HCAPLUS
 (13) Theeuwes; US 4160452 1979 HCAPLUS
 (14) Theeuwes; US 4256108 1981

IT 6493-05-6, Pentoxifylline 6493-05-6D, Pentoxifylline,
 derivs. and metabolites
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological
 study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES
 (Uses)
 (antiproliferative or antifibrotic agents, esp. antisense c-Jun
 oligonucleotides, for treating fibroproliferative diseases)

RN 6493-05-6 HCAPLUS
 CN 1H-Purine-2,6-dione, 3,7-dihydro-3,7-dimethyl-1-(5-oxohexyl)- (9CI) (CA
 INDEX NAME)



RN 6493-05-6 HCAPLUS
 CN 1H-Purine-2,6-dione, 3,7-dihydro-3,7-dimethyl-1-(5-oxohexyl)- (9CI) (CA
 INDEX NAME)



L63 ANSWER 3 OF 25 HCAPLUS COPYRIGHT 2002 ACS
 AN 2001:338333 HCAPLUS
 DN 134:357558
 TI Methods for treating fibroproliferative diseases
 IN Peterson, Theresa C.
 PA Dalhousie University, Can.
 SO PCT Int. Appl., 34 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 IC ICM A61K031-00
 ICS A61K031-522; A61K045-00; A61K045-06; A61K048-00; C12Q001-48;
 G01N033-58; A61P019-04; A61P035-00; A61P037-00; A61P025-28;
 A61P043-00; A61P033-06; A61P031-12; A61P039-00; A61P035-02;

A61P001-00; A61P011-00; A61P013-12; A61P009-00

CC 63-6 (Pharmaceuticals)

Section cross-reference(s): 1, 2, 8, 15

FAN.CNT 4

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001032156	A2	20010510	WO 2000-IB1731	20001102
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	US 6294350	B1	20010925	US 1999-433621	19991102 <--
PRAI	US 1999-433621	A1	19991102		
	US 1997-870096	A2	19970605	<--	
	US 1998-92317	A2	19980605	<--	
AB	In accordance with the present invention, fibroproliferative disease or condition characterized by such symptoms as increased levels of c-Jun homodimers, increased heterodimerization of c-Jun with another signaling peptide, increased levels of phosphorylated c-Jun, or increased presence of Jun kinase are treated by administering to the subject an amt. of a compd. effective to ameliorate one or more of the symptoms of the disease or condition, for example, an antiproliferative or antifibrotic agent. Preferred compds. for administration according to the invention are antisense c-Jun oligonucleotides and compds. that block c-Jun phosphorylation, such as pentoxyfylline, or a functional deriv. or metabolite thereof. Also provided by the present invention are in vitro tests for identifying whether a test compd. is useful for treatment of a subject afflicted with such a disease and kits useful for conducting such assays.				
ST	antiproliferative antisense oligonucleotide fibroproliferative disease cJun				
IT	Peptides, biological studies RL: ADV (Adverse effect, including toxicity); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process) (ATF2; antisense oligonucleotide preps. for treating fibroproliferative diseases)				
IT	Angiotensin receptors RL: BSU (Biological study, unclassified); BIOL (Biological study) (AT1, inhibitors; antisense oligonucleotide preps. for treating fibroproliferative diseases)				
IT	Hepatitis (C; antisense oligonucleotide preps. for treating fibroproliferative diseases)				
IT	Transcription factors RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process) (CREB (cAMP-responsive element-binding); antisense oligonucleotide preps. for treating fibroproliferative diseases)				
IT	Eye, disease Graves' disease (Graves' ophthalmopathy; antisense oligonucleotide preps. for treating fibroproliferative diseases)				
IT	Sarcoma (Kaposi's; antisense oligonucleotide preps. for treating fibroproliferative diseases)				
IT	Neoplasm				

(Li-Fraumeni syndrome; antisense oligonucleotide preps. for treating fibroproliferative diseases)

IT Transcription factors
RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); OCCU (Occurrence) (NF-.kappa.B (nuclear factor .kappa.B); antisense oligonucleotide preps. for treating fibroproliferative diseases)

IT Peptides, biological studies
RL: ADV (Adverse effect, including toxicity); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process) (Nrf1; antisense oligonucleotide preps. for treating fibroproliferative diseases)

IT Eye
(Tenon's capsule, fibroproliferation; antisense oligonucleotide preps. for treating fibroproliferative diseases)

IT Leukemia
(acute myelogenous; antisense oligonucleotide preps. for treating fibroproliferative diseases)

IT Abdomen
(adhesions; antisense oligonucleotide preps. for treating fibroproliferative diseases)

IT Fibrosis
(antifibrotics; antisense oligonucleotide preps. for treating fibroproliferative diseases)

IT Alzheimer's disease
Animal tissue culture
Anti-Alzheimer's agents
 Antitumor agents
 Epithelium
 Fibroblast
 Hematopoietic precursor cell
 Keloid
 Kidney, disease
 Leprosy
 Mesenchyme
 Multiple sclerosis
 Myelodysplastic syndromes
 Myeloproliferative disorders
 Neoplasm
 Neuroglia
 Phosphorylation, biological
 Picrorhiza kurroa
 Signal transduction, biological
 Silicosis
 Silybum marianum
 (antisense oligonucleotide preps. for treating fibroproliferative diseases)

IT Platelet-derived growth factors
 Tumor necrosis factors
RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); OCCU (Occurrence) (antisense oligonucleotide preps. for treating fibroproliferative diseases)

IT Antisense oligonucleotides
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses) (antisense oligonucleotide preps. for treating fibroproliferative diseases)

IT Decorins

Phosphatidylcholines, biological studies
Tocopherols
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (antisense oligonucleotide preps. for treating fibroproliferative diseases)

IT Bronchi
 (bronchiolitis, obliterative; antisense oligonucleotide preps. for treating fibroproliferative diseases)

IT Transcription factors
RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); OCCU (Occurrence)
 (c-jun; antisense oligonucleotide preps. for treating fibroproliferative diseases)

IT Malaria
 (cerebral; antisense oligonucleotide preps. for treating fibroproliferative diseases)

IT Intestine, disease
 (colitis, collagenous; antisense oligonucleotide preps. for treating fibroproliferative diseases)

IT Cardiovascular system
 (disease; antisense oligonucleotide preps. for treating fibroproliferative diseases)

IT Reproductive tract
 (female, **cancer**; antisense oligonucleotide preps. for treating fibroproliferative diseases)

IT Intestine
Lung
Skin
 (fibroblasts of; antisense oligonucleotide preps. for treating fibroproliferative diseases)

IT Radiation
 (fibrosis from; antisense oligonucleotide preps. for treating fibroproliferative diseases)

IT Heart, disease
Kidney, disease
Lung, disease
Peritoneum
 (fibrosis; antisense oligonucleotide preps. for treating fibroproliferative diseases)

IT Neuroglia
 (glioblastoma, sporadic; antisense oligonucleotide preps. for treating fibroproliferative diseases)

IT Neuroglia
 (glioblastoma; antisense oligonucleotide preps. for treating fibroproliferative diseases)

IT Kidney, disease
 (glomerulonephritis; antisense oligonucleotide preps. for treating fibroproliferative diseases)

IT Neutrophil
 (infiltration; antisense oligonucleotide preps. for treating fibroproliferative diseases)

IT Intestine, disease
 (inflammatory; antisense oligonucleotide preps. for treating fibroproliferative diseases)

IT Cytokines
RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); OCCU (Occurrence)
 (inflammatory; antisense oligonucleotide preps. for treating fibroproliferative diseases)

- IT Drug delivery systems
 - (inhalants; antisense oligonucleotide prepns. for treating fibroproliferative diseases)
- IT Drug delivery systems
 - (injections, i.m.; antisense oligonucleotide prepns. for treating fibroproliferative diseases)
- IT Drug delivery systems
 - (injections, i.v.; antisense oligonucleotide prepns. for treating fibroproliferative diseases)
- IT Lung, disease
 - (interstitial; antisense oligonucleotide prepns. for treating fibroproliferative diseases)
- IT Brain, disease
 - (malaria; antisense oligonucleotide prepns. for treating fibroproliferative diseases)
- IT **Antitumor** agents
 - (mammary gland; antisense oligonucleotide prepns. for treating fibroproliferative diseases)
- IT Kidney
 - (mesangium; antisense oligonucleotide prepns. for treating fibroproliferative diseases)
- IT Leukemia
 - (myelogenous; antisense oligonucleotide prepns. for treating fibroproliferative diseases)
- IT Liver
 - (myofibroblasts of; antisense oligonucleotide prepns. for treating fibroproliferative diseases)
- IT Mammary gland
 - (**neoplasm**, inhibitors; antisense oligonucleotide prepns. for treating fibroproliferative diseases)
- IT Mammary gland
 - (**neoplasm**; antisense oligonucleotide prepns. for treating fibroproliferative diseases)
- IT Nerve, **neoplasm**
 - (neuroblastoma; antisense oligonucleotide prepns. for treating fibroproliferative diseases)
- IT Drug delivery systems
 - (oral; antisense oligonucleotide prepns. for treating fibroproliferative diseases)
- IT Proteins, specific or class
 - RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); OCCU (Occurrence)
(p65; antisense oligonucleotide prepns. for treating fibroproliferative diseases)
- IT Phosphatidylcholines, biological studies
 - RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(polyenyl-; antisense oligonucleotide prepns. for treating fibroproliferative diseases)
- IT Proliferation inhibition
 - (proliferation inhibitors; antisense oligonucleotide prepns. for treating fibroproliferative diseases)
- IT Disease, animal
 - (proliferative; antisense oligonucleotide prepns. for treating fibroproliferative diseases)
- IT Drug delivery systems
 - (rectal; antisense oligonucleotide prepns. for treating fibroproliferative diseases)
- IT Connective tissue
 - (scleroderma; antisense oligonucleotide prepns. for treating fibroproliferative diseases)

IT Shock (circulatory collapse)
(septic; antisense oligonucleotide preps. for treating fibroproliferative diseases)

IT Blood vessel
(smooth muscle; antisense oligonucleotide preps. for treating fibroproliferative diseases)

IT Muscle
(smooth; antisense oligonucleotide preps. for treating fibroproliferative diseases)

IT **Carcinoma**
(squamous cell, differentiation disorder; antisense oligonucleotide preps. for treating fibroproliferative diseases)

IT Cell differentiation
(squamous cell, disorder; antisense oligonucleotide preps. for treating fibroproliferative diseases)

IT Drug delivery systems
(sustained-release; antisense oligonucleotide preps. for treating fibroproliferative diseases)

IT Lupus erythematosus
(systemic, nephritis; antisense oligonucleotide preps. for treating fibroproliferative diseases)

IT Drug delivery systems
(topical; antisense oligonucleotide preps. for treating fibroproliferative diseases)

IT Drug delivery systems
(transdermal; antisense oligonucleotide preps. for treating fibroproliferative diseases)

IT Interferons
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(.alpha.; antisense oligonucleotide preps. for treating fibroproliferative diseases)

IT Transforming growth factors
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(.beta.-, RII/FC; antisense oligonucleotide preps. for treating fibroproliferative diseases)

IT 155215-87-5, Jun kinase
RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); OCCU (Occurrence)
(antisense oligonucleotide preps. for treating fibroproliferative diseases)

IT 217308-10-6
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(antisense oligonucleotide preps. for treating fibroproliferative diseases)

IT 50-23-7, Hydrocortisone 54-85-3, Isoniazid 59-67-6, Niacin, biological studies 64-86-8, Colchicine 107-35-7, Taurine 518-34-3, Tetrandrine 1028-33-7, Pentifylline 1405-86-3, Glycyrhizin 6493-05-6, Pentoxifylline 6493-06-7 10102-43-9, Nitric oxide, biological studies 53179-13-8, Pirfenidone 55242-55-2, Propentofylline 55837-20-2, Halofuginone 62571-86-2, Captopril 75847-73-3, Enalapril 80288-49-9, Furafylline 83150-76-9, Octreotide 85721-33-1, Ciprofloxacin 91161-71-6, Terbinafine 114798-26-4, Losartan 119290-87-8, Acanthoic acid 120210-48-2, Tenidap
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES

(Uses)
 (antisense oligonucleotide preps. for treating fibroproliferative diseases)

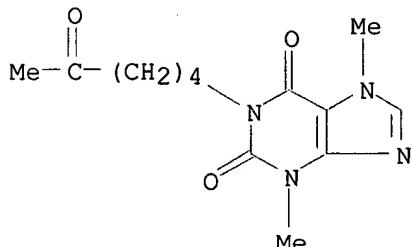
IT 50-88-4, Tritiated thymidine, biological studies 42459-79-0
 RL: BPR (Biological process); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
 (antisense oligonucleotide preps. for treating fibroproliferative diseases)

IT 330196-64-0, Cytochrome p 450 1A2
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
 (inhibitors; antisense oligonucleotide preps. for treating fibroproliferative diseases)

IT 9015-82-1, Angiotensin converting enzyme
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (inhibitors; antisense oligonucleotide preps. for treating fibroproliferative diseases)

IT 6493-05-6, Pentoxifylline
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (antisense oligonucleotide preps. for treating fibroproliferative diseases)

RN 6493-05-6 HCAPLUS
 CN 1H-Purine-2,6-dione, 3,7-dihydro-3,7-dimethyl-1-(5-oxohexyl)- (9CI) (CA INDEX NAME)



L63 ANSWER 4 OF 25 HCAPLUS COPYRIGHT 2002 ACS
 AN 2000:401587 HCAPLUS
 DN 133:26853
 TI Therapeutic uses of protease inhibitors to modulate cellular pathways and immunity
 IN Weichold, Frank F.; Bryant, Joseph L.; Gallo, Robert C.
 PA University of Maryland Biotechnology Institute, USA
 SO PCT Int. Appl., 118 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 IC ICM A01N037-18
 ICS A01N043-04; A61K031-70; A61K038-00; A61K038-48
 CC 1-7 (Pharmacology)
 Section cross-reference(s): 15
 FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI WO 2000033654	A1	20000615	WO 1999-US28548	19991203 <--
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA,				

MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI,
 SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ,
 BY, KG, KZ, MD, RU, TJ, TM
 RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,
 DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,
 CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRAI US 1998-110893P P 19981204 <--

AB The present invention is directed to the use of protease inhibitors, esp. HIV protease, proteasome, serine protease and cysteine protease inhibitors to modulate cellular pathways such as those involved in cell activation, metab., proliferation, differentiation, maturation, cycle, and death. This is useful esp. in the context of **cancer** treatment, allergy, vaccines, autoimmune disorder, inflammation, transplant, burn, trauma, acute ischemia, stroke, aging, wasting syndrome, and infectious conditions. For example, Ritonavir, an HIV protease inhibitor, induced a dose-dependent and reversible inhibition of proliferation of primary endothelial cells (HUVEC) and Kaposi sarcoma cell lines (KS-Y1 and KSIMM). Drug effects on induced apoptosis were dependent on the stage of activation and suggested a relation to cell cycle. Also, susceptibility to activation-induced cell death and apoptosis of T-cells was decreased by Ritonavir by a mechanism that included, but was not limited to, effects on caspase-3 and CD95-dependent apoptosis pathways. The prodn. of apoptosis mediators that are ligands for "death receptors", such as CD95-L and TNF, were inhibited as well.

ST protease inhibitor immunomodulator **antitumor** antiinfective;
 antiinflammatory antiischemic protease inhibitor immunomodulator

IT Selectins

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
 (E-; therapeutic uses of protease inhibitors to modulate cellular pathways and immunity)

IT Antigens

RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
 (HIV gp140 protein; therapeutic uses of protease inhibitors to modulate cellular pathways and immunity)

IT Cell adhesion molecules

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
 (ICAM-1 (intercellular adhesion mol. 1); therapeutic uses of protease inhibitors to modulate cellular pathways and immunity)

IT **Antitumor** agents

(Kaposi's sarcoma; therapeutic uses of protease inhibitors to modulate cellular pathways and immunity)

IT Transcription factors

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
 (NF-.kappa.B (nuclear factor .kappa.B); therapeutic uses of protease inhibitors to modulate cellular pathways and immunity)

IT Transcription factors

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
 (NFAT-1 (nuclear factor, activated T-cell, 1); therapeutic uses of protease inhibitors to modulate cellular pathways and immunity)

IT Cell adhesion molecules

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
 (VCAM-1; therapeutic uses of protease inhibitors to modulate cellular pathways and immunity)

IT Immunostimulants

(adjuvants; therapeutic uses of protease inhibitors to modulate cellular pathways and immunity)

IT Transplant and Transplantation
 Transplant and Transplantation

(bone marrow; therapeutic uses of protease inhibitors to modulate cellular pathways and immunity)

IT Immunity
(disorder; therapeutic uses of protease inhibitors to modulate cellular pathways and immunity)

IT Blood vessel
(endothelium; therapeutic uses of protease inhibitors to modulate cellular pathways and immunity)

IT Envelope proteins
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(gp140env, antigens; therapeutic uses of protease inhibitors to modulate cellular pathways and immunity)

IT T cell (lymphocyte)
(helper cell/inducer, TH1; therapeutic uses of protease inhibitors to modulate cellular pathways and immunity)

IT Blood cell
(homeostasis, inhibition of; therapeutic uses of protease inhibitors to modulate cellular pathways and immunity)

IT Cytokines
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(inflammatory, inhibition of; therapeutic uses of protease inhibitors to modulate cellular pathways and immunity)

IT **Antitumor** agents
(leukemia; therapeutic uses of protease inhibitors to modulate cellular pathways and immunity)

IT Angiogenesis
(neovascularization; therapeutic uses of protease inhibitors to modulate cellular pathways and immunity)

IT Antibodies
RL: BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative)
(neutralizing; therapeutic uses of protease inhibitors to modulate cellular pathways and immunity)

IT Brain, disease
(stroke; therapeutic uses of protease inhibitors to modulate cellular pathways and immunity)

IT Drug interactions
(synergistic; therapeutic uses of protease inhibitors to modulate cellular pathways and immunity)

IT Aging, animal

Allergy inhibitors

Anti-AIDS agents

Anti-infective agents

Anti-inflammatory agents

Anti-ischemic agents

Antibacterial agents

Antitumor agents

Antiviral agents

Apoptosis

Autoimmune disease

Burn

Cell activation

Cell adhesion

Cell cycle

Cell death

Cell differentiation

Cell proliferation

Fungicides

Gene therapy

Hematopoiesis

Hepatitis virus

Human herpesvirus

Human immunodeficiency virus 1
Human immunodeficiency virus 2
Immunomodulators
Immunotherapy
Influenza virus
Malnutrition
Monocyte
Papillomavirus
Parasiticides
Radiation
Radiotherapy
Retroviridae
Shock (circulatory collapse)
Transplant and Transplantation
Transplant rejection
Vaccines
(therapeutic uses of protease inhibitors to modulate cellular pathways and immunity)

IT Tumor necrosis factors
RL: ADV (Adverse effect, including toxicity); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(therapeutic uses of protease inhibitors to modulate cellular pathways and immunity)

IT Chemokines
Fas antigen
Interleukin 10
Interleukin 12
Interleukin 1.beta.
Interleukin 4
Interleukin 5
Interleukin 6
Interleukin 8
Macrophage inflammatory protein 1.alpha.
Monocyte chemoattractant protein-1
RANTES (chemokine)
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(therapeutic uses of protease inhibitors to modulate cellular pathways and immunity)

IT Cytokines
RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(therapeutic uses of protease inhibitors to modulate cellular pathways and immunity)

IT Bone marrow
Bone marrow
Hematopoietic precursor cell
(transplant; therapeutic uses of protease inhibitors to modulate cellular pathways and immunity)

IT Injury
(trauma; therapeutic uses of protease inhibitors to modulate cellular pathways and immunity)

IT Disease, animal
(wasting; therapeutic uses of protease inhibitors to modulate cellular pathways and immunity)

IT Interferons
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(.alpha.; therapeutic uses of protease inhibitors to modulate cellular pathways and immunity)

IT Integrins
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(.alpha.v.beta.3; therapeutic uses of protease inhibitors to modulate cellular pathways and immunity)

IT Interferons
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
 (.beta.1; therapeutic uses of protease inhibitors to modulate cellular pathways and immunity)

IT Interferons
 RL: ADV (Adverse effect, including toxicity); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
 (.gamma.; therapeutic uses of protease inhibitors to modulate cellular pathways and immunity)

IT 144114-21-6, Retropepsin
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
 (therapeutic uses of inhibitors of HIV and other proteases to modulate cellular pathways and immunity)

IT 50-18-0, Cytoxan
 RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
 (therapeutic uses of protease inhibitors to modulate cellular pathways and immunity)

IT 127779-20-8, Saquinavir 133343-34-7, Lactacystin 133407-82-6,
 MG 132 150378-17-9, Indinavir 155213-67-5, Ritonavir 159989-64-7,
 Nelfinavir
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (therapeutic uses of protease inhibitors to modulate cellular pathways and immunity)

IT 9001-92-7, Protease 37259-58-8, Serine protease 37353-41-6, Cysteine protease 122191-40-6, Caspase 1 140879-24-9, Proteasome 169592-56-7, Caspase 3
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
 (therapeutic uses of protease inhibitors to modulate cellular pathways and immunity)

RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD

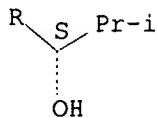
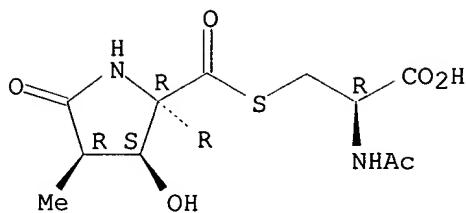
RE
 (1) Hornback; US 5624934 A 1997 HCPLUS

IT 133343-34-7, Lactacystin
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (therapeutic uses of protease inhibitors to modulate cellular pathways and immunity)

RN 133343-34-7 HCPLUS

CN L-Cysteine, N-acetyl-, (2R,3S,4R)-3-hydroxy-2-[(1S)-1-hydroxy-2-methylpropyl]-4-methyl-5-oxo-2-pyrrolidinecarboxylate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



IT 140879-24-9, Proteasome

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
 (therapeutic uses of protease inhibitors to modulate cellular pathways and immunity)

RN 140879-24-9 HCAPLUS

CN Proteinase, multicatalytic (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L63 ANSWER 5 OF 25 HCAPLUS COPYRIGHT 2002 ACS

AN 2000:113042 HCAPLUS

DN 132:161268

TI Therapeutic uses for compounds which reduce c-jun gene expression

IN Peterson, Theresa C.

PA Dalhousie University, Can.

SO U.S., 20 pp., Cont.-in-part of U.S. Ser. No. 870,096.

CODEN: USXXAM

DT Patent

LA English

IC ICM C12Q001-02

NCL 435029000

CC 1-12 (Pharmacology)

Section cross-reference(s): 63

FAN.CNT 4

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6025151	A	20000215	US 1998-92317	19980605 <--
	US 5985592	A	19991116	US 1997-870096	19970605 <--
	CA 2262463	AA	19981210	CA 1998-2262463	19980605 <--
	US 6294350	B1	20010925	US 1999-433621	19991102 <--
PRAI	US 1997-870096	A2	19970605 <--		
	US 1998-92317	A2	19980605 <--		

AB In accordance with the invention, it has been discovered that monocyte conditioned medium (MCM) obtained from patients with liver disease stimulates the proliferation of fibroblasts. Platelet derived growth factor (PDGF) has also been found to stimulate fibroproliferation of fibroblasts, and to be at least partially responsible for the fibroproliferative effect of the MCM. Further, in accordance with the invention, the effect of MCM and PDGF on the expression of c-fos and c-jun has been investigated, because c-fos and c-jun form AP-1 complexes which can stimulate genes involved in proliferation. It has recently been reported that pentoxifylline inhibits platelet derived growth factor-stimulated proliferation. Studies were conducted to det. whether pentoxifylline altered the expression of c-fos and c-jun. While PDGF was found to induce the expression of both c-fos and c-jun, pentoxifylline was

found to effectively reduce the effect of PDGF-induced c-jun gene expression, without altering c-fos gene expression. These results suggest that pentoxifylline inhibits PDGF-stimulated proliferation by decreasing c-jun expression. These results further suggest a variety of diseases and/or conditions which may also be successfully treated with compds., such as pentoxifylline, which reduce the transcription of c-jun gene.

ST jun gene expression inhibition therapeutic; pentoxifylline jun gene expression inhibition therapeutic

IT Platelet-derived growth factors
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (AA; therapeutic uses for compds. which reduce c-jun gene expression, and assocd. methods)

IT Platelet-derived growth factors
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (AB; therapeutic uses for compds. which reduce c-jun gene expression, and assocd. methods)

IT Platelet-derived growth factors
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (BB; therapeutic uses for compds. which reduce c-jun gene expression, and assocd. methods)

IT Eye, disease
 Eye, disease
 Graves' disease
 Graves' disease
 (Graves' ophthalmopathy; therapeutic uses for compds. which reduce c-jun gene expression, and assocd. methods)

IT **Antitumor** agents
 (Kaposi's sarcoma; therapeutic uses for compds. which reduce c-jun gene expression, and assocd. methods)

IT Sarcoma
 (Kaposi's, cell derived from; therapeutic uses for compds. which reduce c-jun gene expression, and assocd. methods)

IT **Neoplasm**
 (Li-Fräumeni syndrome, glioblastoma in; therapeutic uses for compds. which reduce c-jun gene expression, and assocd. methods)

IT Transcription factors
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
 (NF-.kappa.B (nuclear factor .kappa.B); therapeutic uses for compds. which reduce c-jun gene expression, and assocd. methods)

IT **Antitumor** agents
 (acute myelogenous leukemia; therapeutic uses for compds. which reduce c-jun gene expression, and assocd. methods)

IT Gene, animal
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
 (c-fos; therapeutic uses for compds. which reduce c-jun gene expression, and assocd. methods)

IT Gene, animal
 Transcription factors
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
 (c-jun; therapeutic uses for compds. which reduce c-jun gene expression, and assocd. methods)

IT Epithelium
 Mesenchyme
 (cell; therapeutic uses for compds. which reduce c-jun gene expression, and assocd. methods)

IT Drugs
 Ergot (Claviceps)
 (drug-induced ergotism; therapeutic uses for compds. which reduce c-jun gene expression, and assocd. methods)

IT **Antitumor** agents

(female reproductive tract; therapeutic uses for compds. which reduce c-jun gene expression, and assocd. methods)

IT Reproductive tract

Reproductive tract

(female, **neoplasm**, inhibitors; therapeutic uses for compds. which reduce c-jun gene expression, and assocd. methods)

IT Intestine

(fibroblast and smooth muscle cell; therapeutic uses for compds. which reduce c-jun gene expression, and assocd. methods)

IT Skin

(fibroblast; therapeutic uses for compds. which reduce c-jun gene expression, and assocd. methods)

IT Heart, disease

Liver, disease

Lung, disease

(fibrosis; therapeutic uses for compds. which reduce c-jun gene expression, and assocd. methods)

IT Neuroglia

Neuroglia

(glioblastoma, inhibitors; therapeutic uses for compds. which reduce c-jun gene expression, and assocd. methods)

IT **Antitumor** agents

(glioblastoma; therapeutic uses for compds. which reduce c-jun gene expression, and assocd. methods)

IT Kidney, disease

(glomerulonephritis; therapeutic uses for compds. which reduce c-jun gene expression, and assocd. methods)

IT Neutrophil

(infiltration; therapeutic uses for compds. which reduce c-jun gene expression, and assocd. methods)

IT Intestine, disease

(inflammatory; therapeutic uses for compds. which reduce c-jun gene expression, and assocd. methods)

IT Drug delivery systems

(inhalants; therapeutic uses for compds. which reduce c-jun gene expression, and assocd. methods)

IT Drug delivery systems

(injections, i.m.; therapeutic uses for compds. which reduce c-jun gene expression, and assocd. methods)

IT Drug delivery systems

(injections, i.v.; therapeutic uses for compds. which reduce c-jun gene expression, and assocd. methods)

IT Lung, disease

(interstitial; therapeutic uses for compds. which reduce c-jun gene expression, and assocd. methods)

IT Kidney

(mesangium, cell; therapeutic uses for compds. which reduce c-jun gene expression, and assocd. methods)

IT Monocyte

(monocyte conditioned medium; therapeutic uses for compds. which reduce c-jun gene expression, and assocd. methods)

IT **Antitumor** agents

(myelogenous leukemia; therapeutic uses for compds. which reduce c-jun gene expression, and assocd. methods)

IT Fibroblast

(myofibroblast, liver; therapeutic uses for compds. which reduce c-jun gene expression, and assocd. methods)

IT Liver

(myofibroblast; therapeutic uses for compds. which reduce c-jun gene expression, and assocd. methods)

IT Kidney, disease

(nephritis, systemic lupus-assocd.; therapeutic uses for compds. which reduce c-jun gene expression, and assocd. methods)

- IT Cell migration
 - (neutrophil infiltration; therapeutic uses for compds. which reduce c-jun gene expression, and assocd. methods)
- IT Drug delivery systems
 - (oral; therapeutic uses for compds. which reduce c-jun gene expression, and assocd. methods)
- IT Proteins, specific or class
 - RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
 - (p65, NF-.kappa.B p65; therapeutic uses for compds. which reduce c-jun gene expression, and assocd. methods)
- IT Peritoneum
 - (peritoneal fibrosis; therapeutic uses for compds. which reduce c-jun gene expression, and assocd. methods)
- IT Lung
 - (pulmonary fibroblast; therapeutic uses for compds. which reduce c-jun gene expression, and assocd. methods)
- IT Drug delivery systems
 - (rectal; therapeutic uses for compds. which reduce c-jun gene expression, and assocd. methods)
- IT Wound
 - (scar; therapeutic uses for compds. which reduce c-jun gene expression, and assocd. methods)
- IT Connective tissue
 - (scleroderma; therapeutic uses for compds. which reduce c-jun gene expression, and assocd. methods)
- IT Blood vessel
 - (smooth muscle, cell; therapeutic uses for compds. which reduce c-jun gene expression, and assocd. methods)
- IT Muscle
 - (smooth, cell; therapeutic uses for compds. which reduce c-jun gene expression, and assocd. methods)
- IT Drug delivery systems
 - (sustained-release; therapeutic uses for compds. which reduce c-jun gene expression, and assocd. methods)
- IT Drug interactions
 - (synergistic; therapeutic uses for compds. which reduce c-jun gene expression, and assocd. methods)
- IT Lupus erythematosus
 - (systemic, nephritis assocd. with; therapeutic uses for compds. which reduce c-jun gene expression, and assocd. methods)
- IT Anti-Alzheimer's agents
 - Anti-inflammatory agents
 - Antitumor** agents
 - Cardiovascular agents
 - Cell proliferation
 - Fibroblast
 - Hematopoietic precursor cell
 - Kidney, disease
 - Leprosy
 - Myelodysplastic syndromes**
 - Myeloproliferative disorders**
 - Neuroglia
 - (therapeutic uses for compds. which reduce c-jun gene expression, and assocd. methods)
- IT Antisense oligonucleotides
 - RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 - (therapeutic uses for compds. which reduce c-jun gene expression, and assocd. methods)
- IT Cytokines
 - RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological

study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(therapeutic uses for compds. which reduce c-jun gene expression, and assocd. methods)

IT Platelet-derived growth factors
RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(therapeutic uses for compds. which reduce c-jun gene expression, and assocd. methods)

IT Collagens, biological studies
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(therapeutic uses for compds. which reduce c-jun gene expression, and assocd. methods)

IT Interleukin 1
Interleukin 12
Interleukin 4
Tumor necrosis factors
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(therapeutic uses for compds. which reduce c-jun gene expression, and assocd. methods)

IT Drug delivery systems
(topical; therapeutic uses for compds. which reduce c-jun gene expression, and assocd. methods)

IT Drug delivery systems
(transdermal; therapeutic uses for compds. which reduce c-jun gene expression, and assocd. methods)

IT Organ, animal
(transformed cell from; therapeutic uses for compds. which reduce c-jun gene expression, and assocd. methods)

IT Biological transport
(uptake; therapeutic uses for compds. which reduce c-jun gene expression, and assocd. methods)

IT Transforming growth factors
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(.alpha.-; therapeutic uses for compds. which reduce c-jun gene expression, and assocd. methods)

IT Transforming growth factors
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(.beta.-; therapeutic uses for compds. which reduce c-jun gene expression, and assocd. methods)

IT 2610-11-9
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Sirius red; therapeutic uses for compds. which reduce c-jun gene expression, and assocd. methods)

IT 9031-44-1, Kinase 9035-51-2, Cytochrome P 450, biological studies
142008-29-5
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; therapeutic uses for compds. which reduce c-jun gene expression, and assocd. methods)

IT 258852-18-5
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(therapeutic uses for compds. which reduce c-jun gene expression, and assocd. methods)

IT 6493-05-6, Pentoxifylline 6493-05-6D, Pentoxifylline,
derivs. and metabolites 6493-06-7, 1-(5-Hydroxyhexyl)-3,7-
dimethylxanthine 55242-55-2, Propentoxifylline 84477-87-2, H7
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(therapeutic uses for compds. which reduce c-jun gene expression, and assocd. methods)

IT 141436-78-4, Protein kinase C 155215-87-5
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
 (therapeutic uses for compds. which reduce c-jun gene expression, and assocd. methods)

IT 9061-61-4, Nerve growth factor 12777-77-4, Fast green 62229-50-9,
 Epidermal growth factor 67763-96-6, Insulin-like growth factor 1
 67763-97-7, Insulin-like growth factor 2 106096-92-8, Acidic fibroblast
 growth factor 106096-93-9, Basic fibroblast growth factor
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (therapeutic uses for compds. which reduce c-jun gene expression, and assocd. methods)

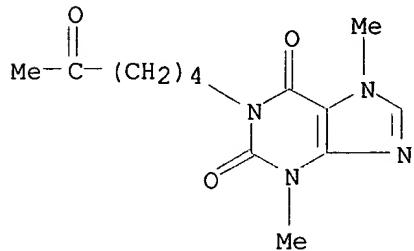
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 US6025151 SEQID: 2 unclaimed DNA
 RL: PRP (Properties)
 (unclaimed nucleotide sequence; therapeutic uses for compds. which reduce c-jun gene expression)

RE.CNT 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD

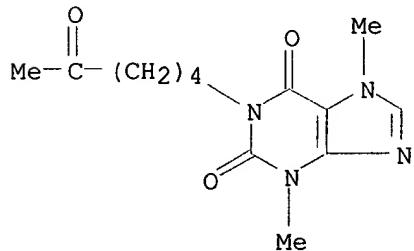
RE

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 IT 6493-05-6, Pentoxifylline 6493-05-6D, Pentoxifylline,
 derivs. and metabolites
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological
 study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES
 (Uses)
 (therapeutic uses for compds. which reduce c-jun gene expression, and
 assocd. methods)
 RN 6493-05-6 HCPLUS
 CN 1H-Purine-2,6-dione, 3,7-dihydro-3,7-dimethyl-1-(5-oxohexyl)- (9CI) (CA
 INDEX NAME)



RN 6493-05-6 HCPLUS
 CN 1H-Purine-2,6-dione, 3,7-dihydro-3,7-dimethyl-1-(5-oxohexyl)- (9CI) (CA
 INDEX NAME)



L63 ANSWER 6 OF 25 HCPLUS COPYRIGHT 2002 ACS
 AN 2000:53374 HCPLUS
 DN 132:102860
 TI Inhibitors of proteasomal activity for stimulating **bone** and hair
 growth
 IN Mundy, Gregory R.; Garrett, I. Ross; Rossini,
 G.
 PA Osteoscreen, USA
 SO PCT Int. Appl., 39 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 IC ICM A61K031-00
 CC 1-12 (Pharmacology)
 Section cross-reference(s): 63
 FAN.CNT 2
 PATENT NO. KIND DATE APPLICATION NO. DATE
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 PI WO 2000002548 A2 20000120 WO 1999-US15533 19990709 <--
 W: AL, AM, AU, BA, BB, BG, BR, CA, CN, CU, CZ, EE, GE, HU, IL, IN,

IS, JP, KP, KR, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ,
 PL, RO, SD, SG, SI, SK, TR, TT, US, UZ, VN, AM, AZ, BY, KG, KZ,
 MD, RU, TJ, TM
 RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK,
 ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG,
 CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
 AU 9963109 A1 20000201 AU 1999-63109 19990709 <--
 EP 1096924 A1 20010509 EP 1999-933827 19990709 <--
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, FI
 PRAI US 1998-113947 A1 19980710 <--
 WO 1999-US15533 W 19990709
 AB Compds. that inhibit the activity of NF-.kappa.B or inhibit the activity
 of the proteasome or both promote **bone** formation and hair growth
 and are thus useful in treating **osteoporosis**, **bone**
fracture or deficiency, primary or secondary
hyperparathyroidism, periodontal disease or defect,
metastatic bone disease, **osteolytic**
bone disease, **post-plastic**
surgery, **post-prosthetic joint surgery**
 , and post-dental implantation. They also stimulate the prodn. of hair
 follicles and are thus useful in stimulating hair growth, including hair
 d., in subject where this is desirable.
 ST hair **bone** growth stimulation NFkappaB inhibitor; proteasome
 inhibitor hair **bone** growth stimulation
 IT Transcription factors
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
 (Biological study); PROC (Process)
 (NF-.kappa.B (nuclear factor .kappa.B); NF-.kappa.B inhibitors and
 inhibitors of proteasomal activity for stimulating **bone** and
 hair growth)
 IT **Bone formation**
 Drug delivery systems
 Drug screening
 (NF-.kappa.B inhibitors and inhibitors of proteasomal activity for
 stimulating **bone** and hair growth)
 IT **Bone morphogenetic proteins**
 Estrogens
 Growth factors, animal
 Hormones, animal, biological studies
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological
 study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES
 (Uses)
 (NF-.kappa.B inhibitors and inhibitors of proteasomal activity for
 stimulating **bone** and hair growth, and use with other agents)
 IT **Antitumor agents**
 (**bone**, metastasis; NF-.kappa.B inhibitors and inhibitors of
 proteasomal activity for stimulating **bone** and hair growth)
 IT **Skull**
 (calvarium, calvarial **bone** growth assay; NF-.kappa.B
 inhibitors and inhibitors of proteasomal activity for stimulating
bone and hair growth)
 IT **Cartilage**
 (cartilage-derived morphogenetic proteins; NF-.kappa.B
 inhibitors and inhibitors of proteasomal activity for stimulating
bone and hair growth, and use with other agents)
 IT **Joint, anatomical**
 (degeneration; NF-.kappa.B inhibitors and inhibitors of proteasomal
 activity for stimulating **bone** and hair growth)
 IT **Disease, animal**
 (dental; NF-.kappa.B inhibitors and inhibitors of proteasomal activity
 for stimulating **bone** and hair growth)
 IT **Periodontium**

(disease; NF-.kappa.B inhibitors and inhibitors of proteasomal activity for stimulating **bone** and hair growth)

IT Hair
(follicle; NF-.kappa.B inhibitors and inhibitors of proteasomal activity for stimulating **bone** and hair growth)

IT Bone, disease
(**fracture**, and **bone** deficiency; NF-.kappa.B inhibitors and inhibitors of proteasomal activity for stimulating **bone** and hair growth)

IT Bone
(growth promoters; NF-.kappa.B inhibitors and inhibitors of proteasomal activity for stimulating **bone** and hair growth, and use with other agents)

IT Hair preparations
(growth stimulants; NF-.kappa.B inhibitors and inhibitors of proteasomal activity for stimulating **bone** and hair growth)

IT Dental materials and appliances
(implants, post-dental implantation; NF-.kappa.B inhibitors and inhibitors of proteasomal activity for stimulating **bone** and hair growth)

IT Cell differentiation
(inducers; NF-.kappa.B inhibitors and inhibitors of proteasomal activity for stimulating **bone** and hair growth, and use with other agents)

IT Bone, neoplasm
(inhibitors, **metastasis**; NF-.kappa.B inhibitors and inhibitors of proteasomal activity for stimulating **bone** and hair growth)

IT Bone, neoplasm
(**metastasis**, inhibitors; NF-.kappa.B inhibitors and inhibitors of proteasomal activity for stimulating **bone** and hair growth)

IT Proteins, specific or class
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(morphogenetic, **cartilage**-derived; NF-.kappa.B inhibitors and inhibitors of proteasomal activity for stimulating **bone** and hair growth, and use with other agents)

IT Growth factors, animal
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**osteogenins**; NF-.kappa.B inhibitors and inhibitors of proteasomal activity for stimulating **bone** and hair growth, and use with other agents)

IT Bone, disease
(**osteolytic**; NF-.kappa.B inhibitors and inhibitors of proteasomal activity for stimulating **bone** and hair growth)

IT Isoprenoids
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(pathway; NF-.kappa.B inhibitors and inhibitors of proteasomal activity for stimulating **bone** and hair growth)

IT Peptides, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(peptidic aldehydes; NF-.kappa.B inhibitors and inhibitors of proteasomal activity for stimulating **bone** and hair growth)

IT Aldehydes, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(peptidyl; NF-.kappa.B inhibitors and inhibitors of proteasomal activity for stimulating **bone** and hair growth)

IT **Surgery**
 (plastic, post-plastic surgery;
 NF-.kappa.B inhibitors and inhibitors of proteasomal activity for stimulating **bone** and hair growth)

IT **Joint, anatomical**
Prosthetic materials and Prosthetics
 (post-prosthetic joint surgery;
 NF-.kappa.B inhibitors and inhibitors of proteasomal activity for stimulating **bone** and hair growth)

IT **Hyperparathyroidism**
 (primary; NF-.kappa.B inhibitors and inhibitors of proteasomal activity for stimulating **bone** and hair growth)

IT **Proteins, specific or class**
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
 (proteasome; NF-.kappa.B inhibitors and inhibitors of proteasomal activity for stimulating **bone** and hair growth)

IT **Bone**
 (resorption, inhibitors; NF-.kappa.B inhibitors and inhibitors of proteasomal activity for stimulating **bone** and hair growth, and use with other agents)

IT **Hyperparathyroidism**
 (secondary; NF-.kappa.B inhibitors and inhibitors of proteasomal activity for stimulating **bone** and hair growth)

IT **Osteoporosis**
 (therapeutic agents; NF-.kappa.B inhibitors and inhibitors of proteasomal activity for stimulating **bone** and hair growth)

IT **Drug delivery systems**
 (topical; NF-.kappa.B inhibitors and inhibitors of proteasomal activity for stimulating **bone** and hair growth)

IT 67-99-2, Gliotoxin 404-86-4, Capsaicin 6493-05-6, Pentoxifylline 59865-13-3, Cyclosporin A 79902-63-9, Simvastatin 106096-93-9, Basic fibroblast growth factor 110044-82-1 110115-07-6 133343-34-7, Lactacystin 133407-82-6, MG 132 133407-86-0, MG 115 158442-41-2 179324-22-2, MG 262
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (NF-.kappa.B inhibitors and inhibitors of proteasomal activity for stimulating **bone** and hair growth)

IT **140879-24-9, Proteasome**
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
 (NF-.kappa.B inhibitors and inhibitors of proteasomal activity for stimulating **bone** and hair growth)

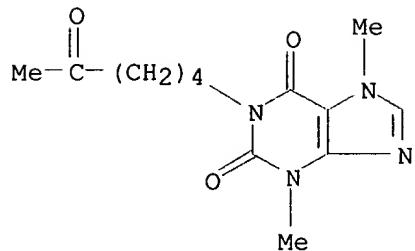
IT 13598-36-2D, Phosphonic acid, bisphosphonates
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (and statins; NF-.kappa.B inhibitors and inhibitors of proteasomal activity for stimulating **bone** and hair growth, and use with other agents)

IT 6493-05-6, Pentoxifylline 133343-34-7, Lactacystin 158442-41-2
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (NF-.kappa.B inhibitors and inhibitors of proteasomal activity for stimulating **bone** and hair growth)

RN 6493-05-6 HCAPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-3,7-dimethyl-1-(5-oxohexyl)- (9CI) (CA)

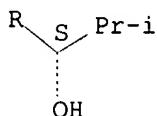
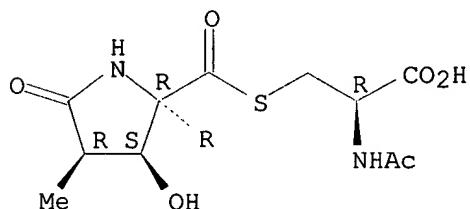
(INDEX NAME)



RN 133343-34-7 HCPLUS

CN L-Cysteine, N-acetyl-, (2R,3S,4R)-3-hydroxy-2-[(1S)-1-hydroxy-2-methylpropyl]-4-methyl-5-oxo-2-pyrrolidinecarboxylate (ester) (9CI) (CA INDEX NAME)

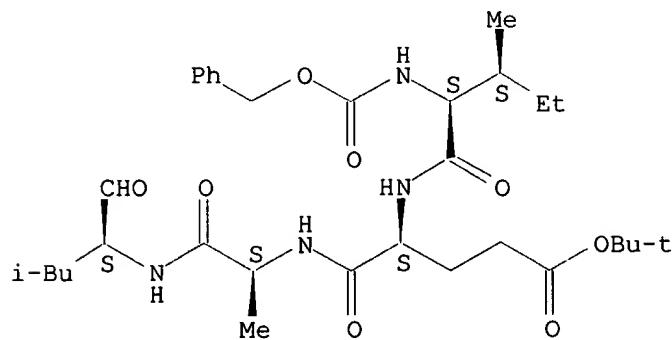
Absolute stereochemistry. Rotation (+).



RN 158442-41-2 HCPLUS

CN L-Alaninamide, N-[(phenylmethoxy)carbonyl]-L-isoleucyl-L-.alpha.-glutamyl-N-[(1S)-1-formyl-3-methylbutyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 140879-24-9, Proteasome

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL

(Biological study); PROC (Process)

(NF-.kappa.B inhibitors and inhibitors of proteasomal activity for stimulating bone and hair growth)

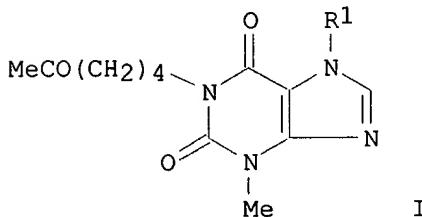
RN 140879-24-9 HCAPLUS
 CN Proteinase, multicatalytic (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L63 ANSWER 7 OF 25 HCAPLUS COPYRIGHT 2002 ACS
 AN 1999:228011 HCAPLUS
 DN 130:306602
 TI Xanthine derivatives for prevention and treatment of **bone** diseases
 IN Takaoka, Kunio
 PA Hoechst Marion Roussel K. K., Japan
 SO Jpn. Kokai Tokkyo Koho, 6 pp.
 CODEN: JKXXAF
 DT Patent
 LA Japanese
 IC ICM A61K031-52
 ICS A61K031-52; C07D473-06
 CC 1-10 (Pharmacology)
 FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI JP 11092379	A2	19990406	JP 1998-216566	19980716 <--
PRAI JP 1997-212713		19970724 <--		

GI



AB Xanthine derivs. (I; R1 = C1-3 straight- or branched-chain alkyl) and their salts, including 1-(5-oxohexyl)-3,7-dimethylxanthine and 1-(5-oxohexyl)-3-methyl-7-propylxanthine, are claimed for prevention and treatment of **bone** diseases, including **osteoporosis**. The effects of I on TNF-.alpha.-induced **bone** resorption and **bone** healing after **fracture** were tested.

ST xanthine deriv **bone** disease TNF alpha; antiosteoporotic xanthine deriv

IT **Bone, disease**
 (fracture; xanthine derivs. for prevention and treatment of **bone** diseases)

IT **Bone**
 (resorption; xanthine derivs. for prevention and treatment of **bone** diseases)

IT **Osteoporosis**
 (therapeutic agents; xanthine derivs. for prevention and treatment of **bone** diseases)

IT **Bone, disease**
 (xanthine derivs. for prevention and treatment of **bone** diseases)

IT **Tumor necrosis factors**
 RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study);

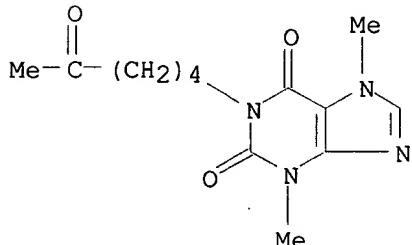
PROC (Process)
 (xanthine derivs. for prevention and treatment of **bone**
 diseases)

IT 69-89-6D, Xanthine, derivs. 6493-05-6, 1-(5-Oxohexyl)-3,7-
 dimethylxanthine 55242-55-2, 1-(5-Oxohexyl)-3-methyl-7-propylxanthine
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological
 study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES
 (Uses)
 (xanthine derivs. for prevention and treatment of **bone**
 diseases)

IT 6493-05-6, 1-(5-Oxohexyl)-3,7-dimethylxanthine
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological
 study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES
 (Uses)
 (xanthine derivs. for prevention and treatment of **bone**
 diseases)

RN 6493-05-6 HCAPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-3,7-dimethyl-1-(5-oxohexyl)- (9CI) (CA
 INDEX NAME)



L63 ANSWER 8 OF 25 HCAPLUS COPYRIGHT 2002 ACS
 AN 1998:761812 HCAPLUS
 DN 130:29195
 TI Therapeutic suppression of **tumor** necrosis factor-.alpha. and
 vascular endothelial growth factor
 IN Feldmann, Marc; Maini, Ravinder Nath; Paleolog, Ewa Maria
 PA The Kennedy Institute of Rheumatology, UK
 SO PCT Int. Appl., 64 pp.
 CODEN: PIXXD2

DT Patent
 LA English
 IC ICM A61K039-395
 ICS A61K031-00; A61K031-505; A61K038-17; A61K031-505
 CC 63-5 (Pharmaceuticals)
 Section cross-reference(s): 1, 15

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9851344	A1	19981119	WO 1998-GB1343	19980512 <--
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU	9873457	A1	19981208	AU 1998-73457	19980512 <--
EP	980258	A1	20000223	EP 1998-920669	19980512 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,				

IE, FI
 JP 2001525816 T2 20011211 JP 1998-548911 19980512 <--
 EP 1170017 A1 20020109 EP 2001-117491 19980512 <--
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, FI
 PRAI US 1997-854881 A 19970512 <--
 EP 1998-920669 A3 19980512 <--
 WO 1998-GB1343 W 19980512 <--
 AB Methods for treating and/or preventing a TNF-mediated disease in an individual are disclosed. Also disclosed are compns. comprising a TNF.alpha. antagonist and a VEGF antagonist. TNF-mediated diseases include rheumatoid arthritis, Crohn's disease, and acute and chronic immune diseases assocd. with transplantation.
 ST **tumor** necrosis factor antibody vascular endothelial growth factor immunosuppressant
 IT Intestine, disease
 (Crohn's; therapeutic suppression of **tumor** necrosis factor-.alpha. and vascular endothelial growth factor)
 IT Immunoglobulins
 RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
 (G, fusion protein with TNF.alpha. receptor; therapeutic suppression of **tumor** necrosis factor-.alpha. and vascular endothelial growth factor)
 IT Antibodies
 RL: BPN (Biosynthetic preparation); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
 (TNF-.alpha.-binding; therapeutic suppression of **tumor** necrosis factor-.alpha. and vascular endothelial growth factor)
 IT Transplant and Transplantation
 (bone marrow; therapeutic suppression of **tumor** necrosis factor-.alpha. and vascular endothelial growth factor)
 IT Antibodies
 RL: BPN (Biosynthetic preparation); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
 (chimeric, cA2, TNF-.alpha.-binding; therapeutic suppression of **tumor** necrosis factor-.alpha. and vascular endothelial growth factor)
 IT Nervous system
 (degeneration; therapeutic suppression of **tumor** necrosis factor-.alpha. and vascular endothelial growth factor)
 IT Immunity
 (disorder; therapeutic suppression of **tumor** necrosis factor-.alpha. and vascular endothelial growth factor)
 IT **Tumor** necrosis factor receptors
 RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
 (fusion protein with IgG; therapeutic suppression of **tumor** necrosis factor-.alpha. and vascular endothelial growth factor)
 IT Transplant and Transplantation
 (heart; therapeutic suppression of **tumor** necrosis factor-.alpha. and vascular endothelial growth factor)
 IT **Tumor** necrosis factors
 RL: ADV (Adverse effect, including toxicity); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
 (inhibitors; therapeutic suppression of **tumor** necrosis factor-.alpha. and vascular endothelial growth factor)
 IT Transplant and Transplantation
 (kidney; therapeutic suppression of **tumor** necrosis factor-.alpha. and vascular endothelial growth factor)

IT Transplant and Transplantation
(liver; therapeutic suppression of **tumor** necrosis factor-.alpha. and vascular endothelial growth factor)

IT Transplant and Transplantation
Transplant and Transplantation
(lung; therapeutic suppression of **tumor** necrosis factor-.alpha. and vascular endothelial growth factor)

IT Transplant and Transplantation
(pancreas; therapeutic suppression of **tumor** necrosis factor-.alpha. and vascular endothelial growth factor)

IT Transplant and Transplantation
(skin; therapeutic suppression of **tumor** necrosis factor-.alpha. and vascular endothelial growth factor)

IT Transplant and Transplantation
Transplant and Transplantation
(small intestine; therapeutic suppression of **tumor** necrosis factor-.alpha. and vascular endothelial growth factor)

IT Intestine
Intestine
(small, transplant; therapeutic suppression of **tumor** necrosis factor-.alpha. and vascular endothelial growth factor)

IT Anti-inflammatory agents
Antirheumatic agents
Autoimmune disease
Immunosuppressants
Inflammation
Rheumatoid arthritis
(therapeutic suppression of **tumor** necrosis factor-.alpha. and vascular endothelial growth factor)

IT Bone marrow
Heart
Kidney
Liver
Lung
Lung
Pancreas
Skin
(transplant; therapeutic suppression of **tumor** necrosis factor-.alpha. and vascular endothelial growth factor)

IT Antibodies
RL: BPN (Biosynthetic preparation); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(vascular endothelial growth factor-binding; therapeutic suppression of **tumor** necrosis factor-.alpha. and vascular endothelial growth factor)

IT 127464-60-2, Vascular endothelial growth factor
RL: ADV (Adverse effect, including toxicity); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(inhibitors; therapeutic suppression of **tumor** necrosis factor-.alpha. and vascular endothelial growth factor)

IT 9025-82-5, Phosphodiesterase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; therapeutic suppression of **tumor** necrosis factor-.alpha. and vascular endothelial growth factor)

IT 50-35-1, Thalidomide 59-05-2, Methotrexate 6493-05-6, Pentoxifylline
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(therapeutic suppression of **tumor** necrosis factor-.alpha. and vascular endothelial growth factor)

RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

- (1) Anon; ARTHRITIS & RHEUMATISM 9 suppl
- (2) Feldmann, M; EUR CYTOKINE NETWORK V8(3), P297 HCPLUS
- (3) Feldmann, M; Int Arch Allergy Immunol 1996, V111(4), P362 HCPLUS
- (4) Genentech Inc; WO 9410202 A 1994 HCPLUS
- (5) Immunex Corp; WO 9406476 A 1994 HCPLUS
- (6) Kavanaugh, A; 60TH NATIONAL SCIENTIFIC MEETING OF THE AMERICAN COLLEGE OF RHEUMATOLOGY AND THE 31ST NATIONAL SCIENTIFIC MEETING OF THE ASSOCIATION OF RHEUMATOLOGY HEALTH PROFESSIONALS 1996
- (7) Kennedy Inst Of Rheumatology; WO 9730088 A 1997 HCPLUS
- (8) Maini Ravinder Nath; WO 9805357 A 1998 HCPLUS
- (9) Univ New York; WO 9216553 A 1992 HCPLUS
- (10) van Deventer, S; CLINICAL NUTRITION (EDINBURGH) 1997, V16(6), P271 HCPLUS

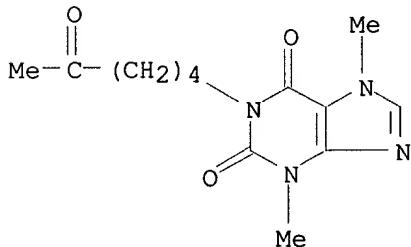
IT 6493-05-6, Pentoxifylline

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(therapeutic suppression of **tumor** necrosis factor-.alpha. and vascular endothelial growth factor)

RN 6493-05-6 HCPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-3,7-dimethyl-1-(5-oxohexyl)- (9CI) (CA INDEX NAME)



L63 ANSWER 9 OF 25 HCPLUS COPYRIGHT 2002 ACS

AN 1998:352416 HCPLUS

DN 129:12439

TI Pentoxifylline synergizes with all-trans retinoic acid to induce differentiation of HL-60 myelocytic cells, but suppresses tRA-augmented clonal growth of normal CFU-GM

AU Yang, Kuender D.; Chao, C. Y.; Shaio, M. F.

CS Children's Hospital, Chang Gung Medical College, Kaohsiung, 833, Taiwan

SO Acta Haematologica (1998), 99(4), 191-199

CODEN: ACHAAH; ISSN: 0001-5792

PB S. Karger AG

DT Journal

LA English

CC 1-6 (Pharmacology)

AB All-trans retinoic acid (tRA) has been shown to promote terminal differentiation of promyelocytic leukemia cells, but frequently induce hyperleukocytosis and pulmonary leakage syndrome. Employing pentoxifylline (PTX), a phosphodiesterase inhibitor which could raise intracellular cAMP and modulate leukocyte activation, we sought to investigate if PTX could enhance tRA-induced promyelocytic leukemic cell differentiation but suppress tRA-augmented growth and activation of human granulocytes. tRA could significantly suppress clonal growth of U937 and HL-60 leukemic cells but enhanced the CFU-GM formation of normal **bone** marrow cells (22 vs. 90 CFU/ well). PTX significantly augmented tRA suppression of clonal growth of U937 and HL-60 leukemic cells but suppressed tRA-augmented CFU-GM formation of normal **bone**

marrow cells (90 vs. 25 CFU/well). In addn., PTX enhanced tRA-induced growth inhibition and differentiation of pro-myelocytic HL-60 leukemic cells, but suppressed respiratory burst activation by the immature granulocytic HL-60 cells and suppressed CD11b adhesion mol. expression by mature granulocytes. PTX similar to dibutyric cAMP promoted HL-60 myelocytic leukemic cell differentiation and growth inhibition, whereas PTX, in contrast to dibutyric cAMP which could augment phorbol myristate acetate (PMA)-elicited respiratory burst activity by immature granulocytes, suppressed the PMA-elicited respiratory burst activity by immature and mature granulocytes. PTX did not raise the intracellular cAMP level of HL-60 cells, but partly suppressed the dibutyric cAMP-elicited elevation of intracellular cAMP level. Results from these studies suggest that PTX might act through different signaling pathways to enhance tRA-induced myelocytic leukemic cell differentiation but prevent from hyperreactive normal granulopoiesis and granulocyte activation.

ST pentoxyfylline synergist retinoic acid cell differentiation
IT Cell differentiation

Leukemia

(pentoxyfylline synergizes with all-trans retinoic acid differentiation of HL-60 cells, but suppresses tRA-augmented clonal growth of normal CFU-GM)

IT 302-79-4, Retinoic acid

RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(all-trans; pentoxyfylline synergizes with all-trans retinoic acid differentiation of HL-60 cells, but suppresses tRA-augmented clonal growth of normal CFU-GM)

IT 6493-05-6, Pentoxyfylline

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(pentoxyfylline synergizes with all-trans retinoic acid differentiation of HL-60 cells, but suppresses tRA-augmented clonal growth of normal CFU-GM)

IT 60-92-4, CAMP

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(pentoxyfylline synergizes with all-trans retinoic acid differentiation of HL-60 cells, but suppresses tRA-augmented clonal growth of normal CFU-GM)

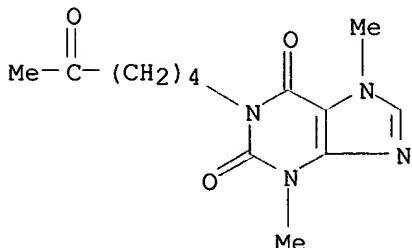
IT 6493-05-6, Pentoxyfylline

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

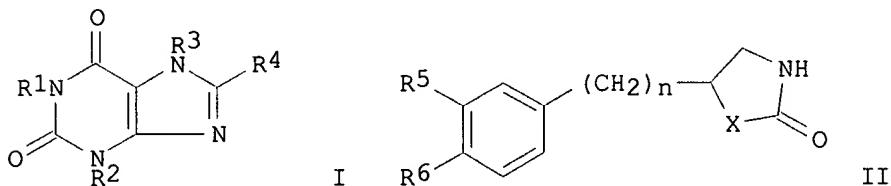
(pentoxyfylline synergizes with all-trans retinoic acid differentiation of HL-60 cells, but suppresses tRA-augmented clonal growth of normal CFU-GM)

RN 6493-05-6 HCAPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-3,7-dimethyl-1-(5-oxohexyl)- (9CI) (CA INDEX NAME)



L63 ANSWER 10 OF 25 HCAPLUS COPYRIGHT 2002 ACS
 AN 1997:556008 HCAPLUS
 DN 127:156735
 TI Phosphodiesterase IV inhibitors for treatment of **osteoporosis**
 IN Miyamoto, Kenichi; Kasugai, Shohei; Waki, Takahiro; Sawanishi, Hiroyuki
 PA Miyamoto, Kenichi, Japan
 SO Jpn. Kokai Tokkyo Koho, 9 pp.
 CODEN: JKXXAF
 DT Patent
 LA Japanese
 IC ICM A61K045-00
 ICS A61K031-40; A61K031-415; A61K031-52; C07D207-26; C07D233-34;
 C07D473-06; C12N009-99
 CC 1-10 (Pharmacology)
 FAN.CNT 1
 PATENT NO. KIND DATE APPLICATION NO. DATE
 ----- ----- ----- -----
 PI JP 09169665 A2 19970630 JP 1995-354850 19951221 <--
 OS MARPAT 127:156735
 GI



AB Phosphodiesterase IV inhibitors I (R1 = H, low alkyloxy, C1-C6 alkyl with or without acyl substitution; R2 = H, low alkyl; R3 = H, low alkyl with or without acyl substitution; R4 = H, C3-C7 cycloalkyl) e.g. xanthine derivs. or II (R5, R6 = low alkyloxy, C3-C7 cycloalkyloxy; n = 0 or 1; X = -CH2- or -NH-) and their pharmaceutical acceptable salts are claimed for treatment of **osteoporosis**. The phosphodiesterase IV-inhibiting and **bone** formation-stimulating actions of I and II were tested.

ST phosphodiesterase IV inhibitor xanthine deriv osteoporosis

IT Bone formation

(phosphodiesterase IV inhibitors for treatment of **osteoporosis**)

IT Osteoporosis

(therapeutic agents; phosphodiesterase IV inhibitors for treatment of osteoporosis)

IT 9036-21-9, Phosphodiesterase IV

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(inhibitors; phosphodiesterase inhibitors)

55-9, biological studies 2850-36-4 6493-05-6 7464-76-8

28822-58-4 29925-17-5 31542-48-0 31542-53-7 31542-62-8
11020 02 2 55212 55 2 57026 71 8 24723 02 4 102146 07 6

41078-02-8 55242-552-2 57076-71-8 94733-93-4 102146-07-6
118024-67-2 121975-96-5 125573-05-9 131627-58-2 135462-05-4

024-617-2 121875-96-5 125573-03-9 131627-58-2 135462-0

135462-18-9 135462-19-0
137386-18-3 138083-27-8

137296-49-2 139093-27-9
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(phosphodiesterase IV inhibitors for treatment of osteoporosis)

IT }

 IT 6493-05-6

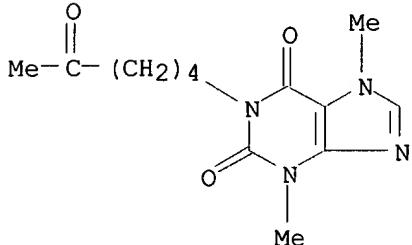
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

 (phosphodiesterase IV inhibitors for treatment of **osteoporosis**)

)

 RN 6493-05-6 HCAPLUS

 CN 1H-Purine-2,6-dione, 3,7-dihydro-3,7-dimethyl-1-(5-oxohexyl)- (9CI) (CA INDEX NAME)



L63 ANSWER 11 OF 25 HCAPLUS COPYRIGHT 2002 ACS

 AN 1997:519052 HCAPLUS

 DN 127:210305

 TI **Tumor** necrosis factor-.alpha. and interleukin-6 release from white blood cells induced by different graft materials in vitro are affected by pentoxifylline and iloprost

 AU Swartbol, P.; Truedsson, L.; Parsson, H.; Norgren, L.

 CS Dep. Surgery, Lund Univ., Lund, S-221 85, Swed.

 SO Journal of Biomedical Materials Research (1997), 36(3), 400-406

 CODEN: JBMRBG; ISSN: 0021-9304

 PB Wiley

 DT Journal

 LA English

 CC 63-7 (Pharmaceuticals)

 Section cross-reference(s): 1

 AB Inflammatory mediators such as cytokines produced by white blood cells (WBCs) at the site of implantation are important for the biocompatibility of vascular grafts. The aim of the present study was to demonstrate the **tumor** necrosis factor-.alpha. (TNF-.alpha.) and interleukin-6 (IL-6) release from WBCs incubated with expanded polytetrafluoroethylene (ePTFE) or woven Dacron grafts. In a second series the effects of pentoxifylline (PTX) and iloprost (ILO), both known to inhibit white blood cell function, on this release were detd. Woven Dacron grafts induced significantly higher release of both TNF-.alpha. and IL-6 compared to ePTFE. TNF-.alpha. was detectable first after 2 h, whereas IL-6 was seen after 4 h. Maximum values were reached at 6 and 12 h, resp. The addn. of an endotoxin gave more pronounced patterns of cytokine release not influenced by time. Preincubation with both PTX and ILO at final concns. of 100 and 10 .mu.g/mL, resp., reduced significantly the TNF-.alpha. release without differences between the two graft materials, whereas the effect on the IL-6 release varied and was graft material-dependent. In conclusion, graft material- dependent induction of TNF-.alpha. and IL-6 from WBCs was demonstrated. PTX and ILO influenced the cytokine release. It might be suggested that graft material-induced cytokine prodn. could contribute to intimal hyperplasia in vivo. The present findings encourage further studies regarding graft material-induced WBC alterations and the role of pharmacol. agents influencing this function.

 ST leukocyte cytokine release vascular implant pentoxifylline; iloprost leukocyte cytokine release vascular implant

IT **Prosthetic materials and Prosthetics**
 (implants, vascular; **tumor** necrosis factor-.alpha. and interleukin-6 release from white blood cells induced by different graft materials in vitro are affected by pentoxifylline and iloprost)

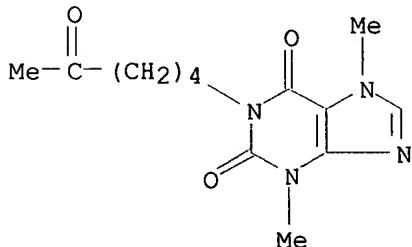
IT Fluoropolymers, biological studies
 Polyester fibers, biological studies
 RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); DEV (Device component use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (tumor necrosis factor-.alpha. and interleukin-6 release from white blood cells induced by different graft materials in vitro are affected by pentoxifylline and iloprost)

IT 9002-84-0, Polytetrafluoroethylene
 RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); DEV (Device component use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (tumor necrosis factor-.alpha. and interleukin-6 release from white blood cells induced by different graft materials in vitro are affected by pentoxifylline and iloprost)

IT 6493-05-6, Pentoxifylline 78919-13-8, Iloprost
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (tumor necrosis factor-.alpha. and interleukin-6 release from white blood cells induced by different graft materials in vitro are affected by pentoxifylline and iloprost)

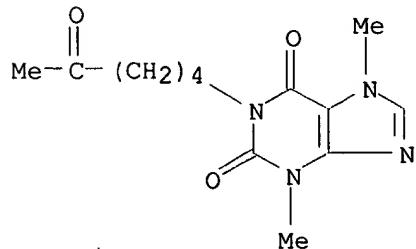
IT 6493-05-6, Pentoxifylline
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (tumor necrosis factor-.alpha. and interleukin-6 release from white blood cells induced by different graft materials in vitro are affected by pentoxifylline and iloprost)

RN 6493-05-6 HCPLUS
 CN 1H-Purine-2,6-dione, 3,7-dihydro-3,7-dimethyl-1-(5-oxohexyl)- (9CI) (CA INDEX NAME)



L63 ANSWER 12 OF 25 HCPLUS COPYRIGHT 2002 ACS
 AN 1997:234397 HCPLUS
 DN 126:311959
 TI Trental effect on collagen proteolysis in experimental aseptic infarction of the long bone
 AU Magomedov, S.; Grigorovskii, V. V.
 CS UNII Travmatol. i Ortoped., MZ Ukrainskii, Kiev, Ukraine
 SO Ukrainskii Biokhimicheskii Zhurnal (1996), 68(5), 69-76
 CODEN: UBZHD4; ISSN: 0201-8470
 PB Naukova Dumka
 DT Journal

LA Russian
 CC 1-8 (Pharmacology)
 AB Dynamics of biochem. parameters of the connective tissue and morphometric parameters of lesion were studied in rabbits with induced embolic aseptic infarction of the femur with and without pentoxyphylline (Trental) treatment. The correlation was found between proteolytic activity and the vol. of bone marrow necrosis, collagenase activity and the rate of regeneration of bone cortex, and the concn. of protein-bound hydroxyproline and a vol. of endosteal regeneration. Trental increased the correlation between the vol. of hydroxyproline fraction and the extent of endosteal regeneration.
 ST Trental collagen proteolysis bone ischemia
 IT Protein degradation
 (Trental effects on collagen proteolysis in exptl. aseptic infarction of long bone)
 IT Collagens, biological studies
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
 (Trental effects on collagen proteolysis in exptl. aseptic infarction of long bone)
 IT Ischemia
 (bone; Trental effects on collagen proteolysis in exptl. aseptic infarction of long bone)
 IT Bone, disease
 (ischemia; Trental effects on collagen proteolysis in exptl. aseptic infarction of long bone)
 IT 6493-05-6, Trental
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (Trental effects on collagen proteolysis in exptl. aseptic infarction of long bone)
 IT 51-35-4, Hydroxyproline 9001-12-1, Collagenase 9047-22-7, Cathepsin b
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
 (Trental effects on collagen proteolysis in exptl. aseptic infarction of long bone)
 IT 6493-05-6, Trental
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (Trental effects on collagen proteolysis in exptl. aseptic infarction of long bone)
 RN 6493-05-6 HCPLUS
 CN 1H-Purine-2,6-dione, 3,7-dihydro-3,7-dimethyl-1-(5-oxohexyl)- (9CI) (CA INDEX NAME)



TI Immune- and inflammation-modulating cytokine-inhibiting agent screening and therapeutic methods

IN Mak, Vivien H. W.

PA De Novo Corp, USA

SO PCT Int. Appl., 129 pp.

CODEN: PIXXD2

DT Patent

LA English

IC ICM A61K045-00

ICS C12N015-00; C12N015-09; C12N015-19; C12Q001-00; C12Q001-66;
G01N033-53

CC 1-1 (Pharmacology)

Section cross-reference(s): 15, 63

FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9527510	A1	19951019	WO 1995-US4677	19950411 <--
	W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT				
	RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9523857	A1	19951030	AU 1995-23857	19950411 <--
	EP 757558	A1	19970212	EP 1995-917009	19950411 <--
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	JP 10500669	T2	19980120	JP 1995-526541	19950411 <--
	EP 937460	A2	19990825	EP 1999-201333	19950411 <--
	EP 937460	A3	20000405		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
	US 5962477	A	19991005	US 1998-97441	19980615 <--
	US 6190691	B1	20010220	US 1998-97440	19980615 <--
PRAI	US 1994-225991	A2	19940412	<--	
	US 1994-271287	A	19940706	<--	
	US 1995-400234	A	19950303	<--	
	EP 1995-917009	A3	19950411	<--	
	WO 1995-US4677	W	19950411	<--	
	US 1995-463819	B1	19950605	<--	

AB Screening methods are provided for evaluating compds. capable of suppressing cytokine prodn. either in vitro or in vivo. The methods generally involve stimulating the prodn. of a cytokine in a cell, exposing a portion of the cells to a putative cytokine-modulating agent, and detg. subsequent levels of cytokine prodn. in the cells. Addnl., the present invention provides certain compds. identified by this method, as well as methods for treating conditions modulated by TNF. The methodol. of the invention may be used for e.g. prevention or redn. of transdermal drug delivery system-induced irritation and treatment of skin or systemic inflammatory conditions. Examples include e.g. inhibition of stimulated cytokine prodn. in human cells by a variety of drugs. Verapamil was effective in preventing the development of skin inflammatory responses in mice.

ST inflammation inhibitor immunomodulator screening; cytokine inhibiting agent screening; therapeutic skin systemic inflammation

IT Lymphokines and Cytokines

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(KC, mRNA for; immune- and inflammation-modulating cytokine-inhibiting agent screening and therapeutic methods)

IT Electric field

(cytokine prodn.-modulating; immune- and inflammation-modulating cytokine-inhibiting agent screening and therapeutic methods)

IT Ribonucleic acids, messenger

RL: BOC (Biological occurrence); BIOL (Biological study); OCCU

(Occurrence)
(for cytokine or MHC class II mol.; immune- and inflammation-modulating cytokine-inhibiting agent screening and therapeutic methods)

IT Acquired immune deficiency syndrome
Animal tissue culture
Antidiabetics and Hypoglycemics
Cachexia
Dermatitis
Immunomodulators
Inflammation inhibitors
Lupus erythematosus
Multiple sclerosis
Psoriasis
Therapeutics
Transcription, genetic
Transplant and Transplantation
(immune- and inflammation-modulating cytokine-inhibiting agent screening and therapeutic methods)

IT Allergens
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(immune- and inflammation-modulating cytokine-inhibiting agent screening and therapeutic methods)

IT Diarrhea
(inhibitors; immune- and inflammation-modulating cytokine-inhibiting agent screening and therapeutic methods)

IT Iontophoresis
(iontophoretic current, cytokine prodn.-modulating; immune- and inflammation-modulating cytokine-inhibiting agent screening and therapeutic methods)

IT Ischemia
(reperfusion; immune- and inflammation-modulating cytokine-inhibiting agent screening and therapeutic methods)

IT Gene
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(reporter; immune- and inflammation-modulating cytokine-inhibiting agent screening and therapeutic methods)

IT Bone
(resorption; immune- and inflammation-modulating cytokine-inhibiting agent screening and therapeutic methods)

IT Ultraviolet radiation
(skin inflammation induced by; immune- and inflammation-modulating cytokine-inhibiting agent screening and therapeutic methods)

IT Cosmetics
(skin sensitization or irritation from; immune- and inflammation-modulating cytokine-inhibiting agent screening and therapeutic methods)

IT Gene, animal
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(transcription frequency; immune- and inflammation-modulating cytokine-inhibiting agent screening and therapeutic methods)

IT Intestine, disease
(Crohn's, immune- and inflammation-modulating cytokine-inhibiting agent screening and therapeutic methods)

IT Glycoproteins, specific or class
RL: BOC (Biological occurrence); BIOL (Biological study); OCCU
(Occurrence)
(ICAM-1 (intercellular adhesion mol. 1), immune- and inflammation-modulating cytokine-inhibiting agent screening and therapeutic methods)

IT Histocompatibility antigens
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(MHC (major histocompatibility antigen complex), class II, immune- and inflammation-modulating cytokine-inhibiting agent screening and

- therapeutic methods)
- IT Respiratory distress syndrome
 - (adult, immune- and inflammation-modulating cytokine-inhibiting agent screening and therapeutic methods)
- IT Bronchodilators
 - (antiasthmatics, immune- and inflammation-modulating cytokine-inhibiting agent screening and therapeutic methods)
- IT Inflammation inhibitors
 - (antirheumatics, immune- and inflammation-modulating cytokine-inhibiting agent screening and therapeutic methods)
- IT Dermatitis
 - (atopic, immune- and inflammation-modulating cytokine-inhibiting agent screening and therapeutic methods)
- IT Ion channel blockers
 - (calcium, immune- and inflammation-modulating cytokine-inhibiting agent screening and therapeutic methods)
- IT Gene
 - RL: BSU (Biological study, unclassified); BIOL (Biological study)
 - (chimeric, immune- and inflammation-modulating cytokine-inhibiting agent screening and therapeutic methods)
- IT Dermatitis
 - (contact, immune- and inflammation-modulating cytokine-inhibiting agent screening and therapeutic methods)
- IT Shock
 - (endotoxin, immune- and inflammation-modulating cytokine-inhibiting agent screening and therapeutic methods)
- IT Transplant and Transplantation
 - (graft-vs.-host reaction, immune- and inflammation-modulating cytokine-inhibiting agent screening and therapeutic methods)
- IT Allergy
 - (hypersensitivity, contact, allergic; immune- and inflammation-modulating cytokine-inhibiting agent screening and therapeutic methods)
- IT Eye, disease
 - (inflammation, immune- and inflammation-modulating cytokine-inhibiting agent screening and therapeutic methods)
- IT Intestine, disease
 - (inflammatory, immune- and inflammation-modulating cytokine-inhibiting agent screening and therapeutic methods)
- IT Lymphokines and Cytokines
 - RL: BOC (Biological occurrence); BPR (Biological process); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
 - (interleukin 1, immune- and inflammation-modulating cytokine-inhibiting agent screening and therapeutic methods)
- IT Lymphokines and Cytokines
 - RL: BSU (Biological study, unclassified); BIOL (Biological study)
 - (interleukin 10, mRNA; immune- and inflammation-modulating cytokine-inhibiting agent screening and therapeutic methods)
- IT Lymphokines and Cytokines
 - RL: BSU (Biological study, unclassified); BIOL (Biological study)
 - (interleukin 1.alpha., mRNA; immune- and inflammation-modulating cytokine-inhibiting agent screening and therapeutic methods)
- IT Lymphokines and Cytokines
 - RL: BOC (Biological occurrence); BIOL (Biological study); OCCU (Occurrence)
 - (interleukin 1.beta., immune- and inflammation-modulating cytokine-inhibiting agent screening and therapeutic methods)
- IT Skin
 - (keratinocyte, immune- and inflammation-modulating cytokine-inhibiting agent screening and therapeutic methods)
- IT Diuretics
 - (loop, immune- and inflammation-modulating cytokine-inhibiting agent screening and therapeutic methods)
- IT Diuretics

(potassium-sparing, immune- and inflammation-modulating cytokine-inhibiting agent screening and therapeutic methods)

IT Perfusion
(re-, immune- and inflammation-modulating cytokine-inhibiting agent screening and therapeutic methods)

IT Pharmaceutical dosage forms
(transdermal, skin adverse reaction from; immune- and inflammation-modulating cytokine-inhibiting agent screening and therapeutic methods)

IT Lymphokines and Cytokines
RL: BOC (Biological occurrence); BPR (Biological process); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(tumor necrosis factor, immune- and inflammation-modulating cytokine-inhibiting agent screening and therapeutic methods)

IT Adrenergic agonists
.beta.-, immune- and inflammation-modulating cytokine-inhibiting agent screening and therapeutic methods)

IT 7440-70-2, Calcium, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(channel, blockers; immune- and inflammation-modulating cytokine-inhibiting agent screening and therapeutic methods)

IT 56-75-7, Chloramphenicol 9014-00-0, Luciferase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(gene; immune- and inflammation-modulating cytokine-inhibiting agent screening and therapeutic methods)

IT 50-35-1, Thalidomide 50-52-2, Thioridazine 51-41-2, Arterenol
52-01-7, Spironolactone 52-53-9, Verapamil 54-31-9, Furosemide
915-30-0, Diphenoxylate 1143-38-0, Dithranol 1214-79-5 1845-11-0,
Nafoxidine 2062-78-4, Pimozide 2609-46-3, Amiloride 6493-05-6
, Pentoxyfylline 10540-29-1, Tamoxifen 21829-25-4, Nifedipine
23031-25-6, Terbutaline 29925-17-5, RO 20-1724 36622-29-4,
(-)-Verapamil 38321-02-7, (+)-Verapamil 42399-41-7, Diltiazem
52468-60-7, Flunarizine 53179-11-6, Loperamide 55985-32-5, Nicardipine
64706-54-3, Bepridil 66085-59-4, Nimodipine 75695-93-1, Isradipine
100427-26-7, Rec 15/2375
RL: BAC (Biological activity or effector, except adverse); THU
(Therapeutic use); BIOL (Biological study); USES (Uses)
(immune- and inflammation-modulating cytokine-inhibiting agent screening and therapeutic methods)

IT 58-94-6D, Thiazide, derivs. 140-29-4D, Benzeneacetonitrile, derivs.
27790-75-6D, Dihydropyridine, derivs. 73087-48-6D, 1,5-Benzothiazepin-4(5H)-one, derivs.
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(immune- and inflammation-modulating cytokine-inhibiting agent screening and therapeutic methods)

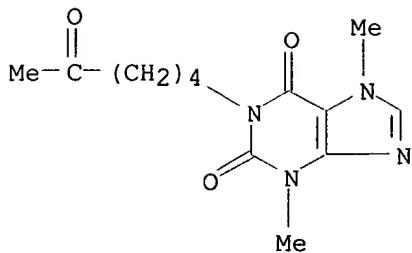
IT 9025-82-5, Phosphodiesterase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; immune- and inflammation-modulating cytokine-inhibiting agent screening and therapeutic methods)

IT 302-79-4, Retin-A
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(skin inflammation from; immune- and inflammation-modulating cytokine-inhibiting agent screening and therapeutic methods)

IT 6493-05-6, Pentoxyfylline
RL: BAC (Biological activity or effector, except adverse); THU
(Therapeutic use); BIOL (Biological study); USES (Uses)
(immune- and inflammation-modulating cytokine-inhibiting agent screening and therapeutic methods)

RN 6493-05-6 HCAPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-3,7-dimethyl-1-(5-oxohexyl)- (9CI) (CA INDEX NAME)



L63 ANSWER 14 OF 25 HCPLUS COPYRIGHT 2002 ACS
 AN 1995:624053 HCPLUS
 DN 123:40874
 TI Regulation of collagen and glycosaminoglycan biosynthesis by human breast implant capsule fibroblasts by interferons-alpha, -beta and -gamma and pentoxifylline
 AU Duncan, Matthew R.; Berman, Brian; Cedars, Michael G.
 CS Fr.
 SO Eur. J. Dermatol. (1995), 5(2), 156-9
 CODEN: EJDEE4; ISSN: 1167-1122
 DT Journal
 LA English
 CC 63-7 (Pharmaceuticals)
 Section cross-reference(s): 15
 AB To det. the therapeutic potential of interferon (IFN) and pentoxifylline treatment for breast implant capsule contractures, we investigated the effect of human recombinant (hu-r) IFNs and pentoxifylline on cultured fibroblasts derived from a fibrotic capsule which developed around an implanted breast **prosthesis**. Treatment of cultured fibroblasts with hu-r-IFN-alpha2b, hu-r-IFN-beta-ser17 or hu-r-IFN-gamma resulted in reduced fibroblast collagen prodn. Hu-r-IFN-alpha and -beta inhibited fibroblast glycosaminoglycan (GAG) prodn., while hu-r-IFN-gamma increased GAG prodn. Pentoxifylline treatment of cultured breast implant capsule fibroblasts markedly inhibited their collagen and GAG prodn. These results demonstrate that IFNs, esp. IFNs-alpha and -beta, and pentoxifylline exhibit antifibrotic activity on breast implant capsule fibroblasts and suggest a rationale for using these agents to treat breast implant capsule fibrosis, a specific form of post-surgical scarring.
 ST breast implant capsule fibroblast collagen glycosaminoglycan; interferon pentoxifylline collagen glycosaminoglycan fibroblast
 IT Fibroblast
 (interferons and pentoxifylline regulation of collagen and glycosaminoglycan biosynthesis by human breast implant capsule fibroblasts)
 IT Collagens, biological studies
 Glycosaminoglycans, biological studies
 RL: MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative)
 (interferons and pentoxifylline regulation of collagen and glycosaminoglycan biosynthesis by human breast implant capsule fibroblasts)
 IT Mammary gland
 (artificial, interferons and pentoxifylline regulation of collagen and glycosaminoglycan biosynthesis by human breast implant capsule fibroblasts)
 IT Mammary gland
 (disease, fibrosis; interferons and pentoxifylline regulation of collagen and glycosaminoglycan biosynthesis by human breast implant capsule fibroblasts)
 IT **Prosthetic** materials and **Prosthetics**
 (implants, interferons and pentoxifylline regulation of collagen and

glycosaminoglycan biosynthesis by human breast implant capsule fibroblasts)

IT Interferons
 RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (.alpha.2, human recombinant; interferons and pentoxyfylline regulation of collagen and glycosaminoglycan biosynthesis by human breast implant capsule fibroblasts)

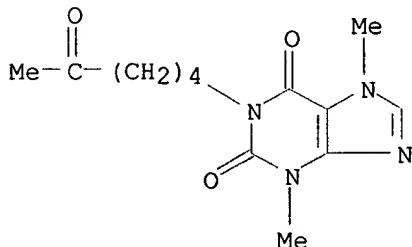
IT Interferons
 RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (.beta., human recombinant; interferons and pentoxyfylline regulation of collagen and glycosaminoglycan biosynthesis by human breast implant capsule fibroblasts)

IT Interferons
 RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (.gamma., human recombinant; interferons and pentoxyfylline regulation of collagen and glycosaminoglycan biosynthesis by human breast implant capsule fibroblasts)

IT 6493-05-6, Pentoxyfylline
 RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (interferons and pentoxyfylline regulation of collagen and glycosaminoglycan biosynthesis by human breast implant capsule fibroblasts)

IT 6493-05-6, Pentoxyfylline
 RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (interferons and pentoxyfylline regulation of collagen and glycosaminoglycan biosynthesis by human breast implant capsule fibroblasts)

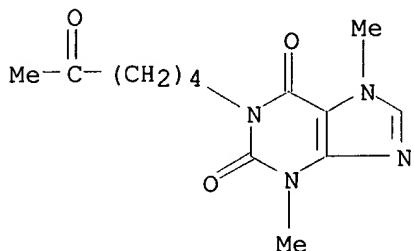
RN 6493-05-6 HCPLUS
 CN 1H-Purine-2,6-dione, 3,7-dihydro-3,7-dimethyl-1-(5-oxohexyl)- (9CI) (CA INDEX NAME)



L63 ANSWER 15 OF 25 HCPLUS COPYRIGHT 2002 ACS
 AN 1995:519036 HCPLUS
 DN 122:274087
 TI Chewable delayed-release tablet
 IN Korsatko, Werner; Korsatko, Brigitte; Tritthart, Wolfram
 PA Austria
 SO Ger. Offen., 10 pp.
 CODEN: GWXXBX
 DT Patent
 LA German
 IC ICM A61K009-22
 ICS A61K033-16; A61K033-06
 CC 63-6 (Pharmaceuticals)
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 4333190	A1	19950330	DE 1993-4333190	19930929 <--
	DE 4333190	C2	19960530		
	WO 9508988	A1	19950406	WO 1994-EP3166	19940922 <--
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	AU 9478088	A1	19950418	AU 1994-78088	19940922 <--
	EP 715515	A1	19960612	EP 1994-928795	19940922 <--
	R: AT, BE, CH, DE, ES, FR, GB, IT, LI, NL, PT				
PRAI	DE 1993-4333190		19930929 <--		
	WO 1994-EP3166		19940922 <--		
AB	A delayed-release tablet comprises a chewable mass contg. active ingredient in microparticles which are not disrupted during chewing, owing to their strength and elasticity. The microparticles may have a matrix of Eudragit or cellulose deriv. and a shell of the same materials. Thus, tablets based on tri-Ca citrate, citric acid, sorbitol, aspartame, orange flavoring, and Mg stearate and contg. microparticles composed of Na monofluorophosphate 42.0, lactose 8.0, Avicel PH101 27.0, Methocel K100 8.0, hydroxypropylmethylcellulose phthalate 12.0, and di-Et phthalate (plasticizer) 3.0% released active substance over a period of 6 h.				
ST	delayed release chewable tablet; Eudragit delayed release chewable tablet; cellulose deriv delayed release chewable tablet				
IT	Allergy inhibitors Antihypertensives Circulation Diuretics Inflammation inhibitors Osteoporosis Plasticizers Vasodilators (chewable delayed-release tablet)				
IT	Antihistaminics (H2, chewable delayed-release tablet)				
IT	Inflammation inhibitors (antirheumatics, chewable delayed-release tablet)				
IT	Pharmaceutical dosage forms (microparticles, chewable delayed-release tablet)				
IT	Pharmaceutical dosage forms (tablets, delayed-release, chewable delayed-release tablet)				
IT	Adrenergic antagonists (.alpha.-, chewable delayed-release tablet)				
IT	Adrenergic antagonists (.beta.-, chewable delayed-release tablet)				
IT	54-31-9, Furosemide 58-93-5, Hydrochlorothiazide 471-34-1, Calcium carbonate, biological studies 525-66-6, Propranolol 813-94-5, Tricalcium citrate 1185-56-4 3200-06-4 4205-90-7, Clonidine 6493-05-6, Pentoxyfylline 7440-70-2D, Calcium, complexes and salts 7681-49-4, Sodium fluoride, biological studies 10103-46-5, Calcium phosphate 10163-15-2, Sodium monofluorophosphate 15307-79-6, Diclofenac sodium 15307-86-5, Diclofenac 29122-68-7, Atenolol 31329-57-4D, Naftidrofuryl, salts 51481-61-9, Cimetidine 66357-35-5, Ranitidine 79794-75-5, Loratadine				
	RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (chewable delayed-release tablet)				
IT	9004-34-6, Avicel PH 101, biological studies 9004-34-6D, Cellulose, derivs. 9004-38-0, Cellulose acetate phthalate 9004-57-3, Ethylcellulose 9004-62-0, Hydroxyethylcellulose 9004-64-2, Hydroxypropylcellulose 9004-67-5, Methylcellulose 9050-31-1, Hydroxypropylmethylcellulose phthalate 9065-11-6, Eudragit 25086-15-1, Eudragit S 100 25212-88-8 33434-24-1, Eudragit RS RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)				

(chewable delayed-release tablet)
 IT 77-93-0, Triethyl citrate 84-66-2, Diethyl phthalate 84-74-2, Dibutyl phthalate
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (plasticizer; chewable delayed-release tablet)
 IT 6493-05-6, Pentoxifylline
 RL: BAC (Biological activity or effector, except adverse); THU
 (Therapeutic use); BIOL (Biological study); USES (Uses)
 (chewable delayed-release tablet)
 RN 6493-05-6 HCAPLUS
 CN 1H-Purine-2,6-dione, 3,7-dihydro-3,7-dimethyl-1-(5-oxohexyl)- (9CI) (CA INDEX NAME)



L63 ANSWER 16 OF 25 HCAPLUS COPYRIGHT 2002 ACS
 AN 1995:227140 HCAPLUS
 DN 122:151367
 TI Compounds for treatment of proliferative diseases mediated by second messengers
 IN Leigh, Alistair; Michnick, John; Kumar, Anil; Underiner, Gail; Rice, Glenn C.; Klein, J. Peter; Reddy, Dandu
 PA Cell Therapeutics, Inc., USA
 SO PCT Int. Appl., 68 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 IC ICM A61K031-52
 ICS A61K031-40; C07D473-06; C07D473-34; C07D403-12; C07D413-14;
 C07D031-495; C07D031-505
 CC 1-6 (Pharmacology)
 Section cross-reference(s): 10, 28
 FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9422449	A1	19941013	WO 1994-US3610	19940401 <--
	W: AU, CA, JP RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	US 5670506	A	19970923	US 1993-42946	19930405 <--
	AU 9466238	A1	19941024	AU 1994-66238	19940401 <--
	EP 714302	A1	19960605	EP 1994-914005	19940401 <--
	R: DE, FR, GB, IT				
PRAI	US 1993-42946		19930405 <--		
	WO 1994-US3610		19940401 <--		
OS	MARPAT 122:151367				
AB	Carbocyclic and heterocyclic compds. with 5-7 ring atoms are prep'd. which are useful as antiproliferative agents for treatment and prevention of diseases mediated by 2nd-messenger pathways. Thus, 1-(6-chloro-5-oxohexyl)-3,7-dimethylxanthine at 100 .mu.M inhibited by 88% the degranulation of mast cells in response to allergen challenge and strongly inhibited growth of <i>Saccharomyces cerevisiae</i> , an indication of potential topical or systemic antimicrobial activity.				

ST cytostatic heterocyclic compd; antimicrobial heterocyclic compd
IT Acquired immune deficiency syndrome
Allergy inhibitors
Alopecia
Antidiabetics and Hypoglycemics
Autoimmune disease
Cytotoxic agents
Fungicides and Fungistats
Immunosuppressants
Lupus erythematosus
Multiple sclerosis
 Neoplasm inhibitors
 Osteoporosis
Psoriasis
Sepsis and Septicemia
 (compds. for treatment of proliferative diseases mediated by second messengers)
IT Cyclic compounds
Heterocyclic compounds
Lactams
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (compds. for treatment of proliferative diseases mediated by second messengers)
IT Basophil
Mast cell
 (degranulation; compds. for treatment of proliferative diseases mediated by second messengers)
IT Blood vessel
 (formation of; compds. for treatment of proliferative diseases mediated by second messengers)
IT Signal transduction, biological
 (inhibition of IL-.beta.-induced; compds. for treatment of proliferative diseases mediated by second messengers)
IT Transplant and Transplantation
 (rejection; compds. for treatment of proliferative diseases mediated by second messengers)
IT Acquired immune deficiency syndrome
 (-related complex, compds. for treatment of proliferative diseases mediated by second messengers)
IT Hepatitis
 (alc., compds. for treatment of proliferative diseases mediated by second messengers)
IT Inflammation inhibitors
 (antiarthritics, compds. for treatment of proliferative diseases mediated by second messengers)
IT Bronchodilators
 (antiasthmatics, compds. for treatment of proliferative diseases mediated by second messengers)
IT Antiarteriosclerotics
 (antiatherosclerotics, compds. for treatment of proliferative diseases mediated by second messengers)
IT Thyroid gland, disease
 (autoimmune thyroiditis, compds. for treatment of proliferative diseases mediated by second messengers)
IT Artery, disease
 (coronary, compds. for treatment of proliferative diseases mediated by second messengers)
IT Mental disorder
 (dementia, HIV-assocd.; compds. for treatment of proliferative diseases mediated by second messengers)
IT Periodontium

(disease, compds. for treatment of proliferative diseases mediated by second messengers)

IT Connective tissue
 (disease, scleroderma, compds. for treatment of proliferative diseases mediated by second messengers)

IT Sleep
 (disorder, compds. for treatment of proliferative diseases mediated by second messengers)

IT Parturition
 (disorder, premature, secondary to uterine infection; compds. for treatment of proliferative diseases mediated by second messengers)

IT Kidney, disease
 (glomerulonephritis, compds. for treatment of proliferative diseases mediated by second messengers)

IT Quaternary ammonium compounds, biological studies
 RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (heterocyclic, compds. for treatment of proliferative diseases mediated by second messengers)

IT Uterus, disease
 (infection, premature parturition secondary to; compds. for treatment of proliferative diseases mediated by second messengers)

IT Intestine, disease
 (inflammatory, compds. for treatment of proliferative diseases mediated by second messengers)

IT Lymphokines and Cytokines
 RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
 (interleukin 1.beta., antagonists; compds. for treatment of proliferative diseases mediated by second messengers)

IT Neoplasm inhibitors
 (myelogenous leukemia, compds. for treatment of proliferative diseases mediated by second messengers)

IT Heterocyclic compounds
 RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (nitrogen, compds. for treatment of proliferative diseases mediated by second messengers)

IT Artery, disease
 (restenosis, compds. for treatment of proliferative diseases mediated by second messengers)

IT Shock
 (septic, compds. for treatment of proliferative diseases mediated by second messengers)

IT Brain, disease
 (stroke, compds. for treatment of proliferative diseases mediated by second messengers)

IT 53-86-1DP, Indomethacin, derivs. 55-21-0DP, Benzamide, derivs.
 65-71-4DP, Thymine, derivs. 65-86-1DP, Orotic acid, derivs. 66-22-8DP, Uracil, derivs. 67-52-7DP, Barbituric acid, derivs. 69-72-7DP, Salicylic acid, derivs. 69-89-6DP, Xanthine, derivs. 69-93-2DP, Uric acid, derivs. 71-43-2DP, Benzene, derivs. 79-77-6DP, .beta.-Ionone, derivs. 83-67-0DP, Theobromine, derivs. 85-41-6DP, Phthalimide, derivs. 91-18-9DP, Pteridine, derivs. 91-20-3DP, Naphthalene, derivs. 91-21-4DP, derivs. 91-22-5DP, Quinoline, derivs. 92-52-4DP, Biphenyl, derivs. 106-51-4DP, 2,5-Cyclohexadiene-1,4-dione, derivs. 108-46-3DP, 1,3-Benzenediol, derivs. 109-97-7DP, Pyrrole, amides 110-82-7DP, Cyclohexane, derivs. 110-86-1DP, Pyridine, derivs. 110-89-4DP, Piperidine, derivs. 123-56-8DP, Succinimide, derivs. 132-86-5DP, 1,3-Dihydroxynaphthalene, derivs. 142-08-5DP, 2-Hydroxypyridine, derivs. 288-32-4DP, Imidazole, derivs. 289-95-2DP, Pyrimidine, derivs. 472-66-2DP, 2,6,6-Trimethyl-1-cyclohexene-1-acetaldehyde, derivs.

487-21-8DP, Lumazine, derivs. 491-30-5DP, 1(2H)-Isoquinolinone, derivs.
 491-36-1DP, Quinazolin-4(3H)-one, derivs. 588-59-0DP, Stilbene, derivs.
 611-59-6DP, 1,7-Dimethylxanthine, derivs. 615-77-0DP, 1-Methyluracil,
 derivs. 696-04-8DP, Dihydrothymine, derivs. 696-11-7DP,
 1-Methyl-5,6-dihydrouracil, derivs. 1006-08-2DP, 7-Methylhypoxanthine,
 derivs. 1076-22-8DP, 3-Methylxanthine, derivs. 1121-89-7DP,
 Glutarimide, derivs. 1123-40-6DP, 3,3-Dimethylglutarimide, derivs.
 1406-18-4DP, Vitamin E, derivs. 1444-94-6DP, Hexahydrophthalimide,
 derivs. 4456-77-3DP, Homophthalimide, derivs. 11103-57-4DP, Vitamin A,
 derivs. 12001-79-5DP, Vitamin K, derivs. 12654-97-6DP, Triazine,
 derivs. 27813-21-4DP, Tetrahydrophthalimide, derivs. 27942-00-3DP,
 Methyluracil, derivs. 28473-29-2DP, Cyclopentanedione, derivs.
 29059-07-2DP, Tetralone, derivs. 30581-70-5DP, Cyclohexanedione, derivs.
 35121-78-9DP, Prostacyclin, derivs. 38194-50-2DP, Sulindac, derivs.
 50256-18-3DP, 1-Methylllumazine, derivs. 53126-65-1DP, Tricyclododecane,
 derivs. 56395-76-7P 79012-66-1P 93667-91-5P 109421-37-6DP, derivs.
 159431-45-5DP, derivs. 159431-46-6DP, derivs. 159431-47-7P
 159431-48-8P 159431-49-9P 159431-50-2P 159431-51-3P 159431-52-4P
 159431-53-5P 159431-54-6P 159431-55-7P 159431-56-8P 159431-57-9P
 159431-58-0P 159431-59-1P 159431-60-4P 159431-61-5P 159431-62-6P
 159431-63-7P 159431-64-8P 159431-65-9P 159431-66-0P 159431-67-1P
 159431-68-2P 159431-69-3P 159431-70-6P 159431-71-7P 159431-72-8P
 161098-93-7DP, derivs. 161098-94-8DP, derivs. 161271-41-6DP,
 2H-Quinolizinedione, derivs.

RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(compds. for treatment of proliferative diseases mediated by second messengers)

IT 83-67-0, Theobromine 86-96-4, Benzoyleneurea 2695-47-8,
 1-Bromo-5-hexene 2695-48-9, 8-Bromo-1-octene 4160-72-9,
 1-Methylthymine 4286-55-9 6493-05-6, Pentoxifylline
 13019-22-2, 9-Decen-1-ol 89359-54-6, 9-Bromo-1-nonene 159431-78-4

RL: RCT (Reactant)

(compds. for treatment of proliferative diseases mediated by second messengers)

IT 604-50-2P 6493-06-7P 38975-41-6P 56395-71-2P 58999-18-1P
 114640-35-6P 154719-57-0P 154755-53-0P 156918-08-0P 156918-13-7P
 156918-28-4P 156918-35-3P 156918-57-9P 157523-33-6P 159431-73-9P
 159431-74-0P 159431-75-1P 159431-76-2P 159431-77-3P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)

(compds. for treatment of proliferative diseases mediated by second messengers)

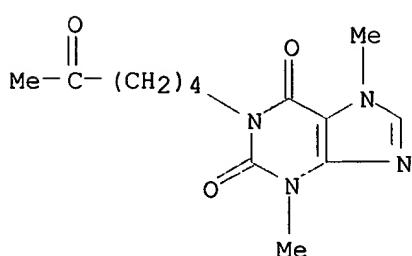
IT 6493-05-6, Pentoxifylline

RL: RCT (Reactant)

(compds. for treatment of proliferative diseases mediated by second messengers)

RN 6493-05-6 HCAPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-3,7-dimethyl-1-(5-oxohexyl)- (9CI) (CA INDEX NAME)



L63 ANSWER 17 OF 25 HCPLUS COPYRIGHT 2002 ACS
 AN 1994:622027 HCPLUS
 DN 121:222027
 TI Oxime-substituted therapeutic compounds for diseases mediated by intracellular signaling
 IN Leigh, Alistair; Klein, J. Peter
 PA Cell Therapeutics, Inc., USA
 SO PCT Int. Appl., 68 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 IC ICM A61K031-52
 CC 1-12 (Pharmacology)
 Section cross-reference(s): 28
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9416704	A1	19940804	WO 1994-US763	19940119 <--
	W: AU, CA, JP, NZ RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE AU 9460927	A1	19940815	AU 1994-60927	19940119 <--
PRAI	US 1993-6083		19930119 <--		
	WO 1994-US763		19940119 <--		
OS	MARPAT 121:222027				
AB	Oxime-substituted compds., preferably cyclic or heterocyclic compds, are disclosed which are useful in a large variety of therapeutic indications for treating or preventing disease mediated by intracellular signaling through specific intracellular signaling pathways. The oxime-substituted compds., and pharmaceutical compns. thereof, have the formula core moiety-(R) ^j [j = 1-3; core moiety = cyclic, noncyclic; R = H, halo, OH, amino, (substituted) C1-10 alkyl, C2-10 alkenyl, (hetero)cyclyl, (CH ₂) _n C(R ₁) _p (.gtoreq.1 R is (CH ₂) _n C(R ₁) _p) (n = 3-20; p = 2,3; R ₁ = H, halo, OH, (substituted) C1-10 alkyl, C1-10 ether, C2-10 alkenyl, (hetero)cyclyl, :NOR2 (R ₂ = H, (substituted) C1-10 alkyl, C2-10 alkenyl, (hetero)cyclyl), (CH ₂) _s C(R ₃) _t (s = 0-10; t = 2,3; R ₃ = H, halo, OH, (substituted) C1-10 alkyl, C1-10 ether, C2-10 alkenyl, (hetero)cyclyl, :NOR2 (R ₂ as above)); .gtoreq.1 R ₁ or 1 R ₃ = :NOR2 (p or t corresponding to the .gtoreq.1 R ₁ or 1 R ₃ being 2); second R ₁ or R ₃ , bonded to same C as the .gtoreq.1 R ₁ or 1 R ₃ , is other than :NOR2)], including resolved enantiomers (both syn and anti forms) and/or diastereomers, hydrates, salts, solvates and mixts. thereof. Oxime-substituted dimethylxanthines were prep'd. and tested for inhibition of thymocyte proliferation, for mixed lymphocyte reaction, etc.; 8 specific compds. are claimed. The compds. of the invention can be used in the treatment of inflammatory diseases, asthma, atherosclerosis, AIDS, malignancies , septic shock, sleep disorders, etc.				
ST	oxime deriv therapeutic; dimethylxanthine oxime deriv therapeutic; signal transduction therapeutic oxime deriv; xanthine dimethyl oxime deriv therapeutic				
IT	Acquired immune deficiency syndrome Allergy inhibitors Alopecia Antidiabetics and Hypoglycemics Blood vessel Inflammation inhibitors Lupus erythematosus Multiple sclerosis Neoplasm inhibitors Osteoporosis Psoriasis Signal transduction, biological Therapeutics				

(oxime-substituted therapeutic compds. for diseases mediated by intracellular signaling)

IT Transplant and Transplantation
(rejection; oxime-substituted therapeutic compds. for diseases mediated by intracellular signaling)

IT Acquired immune deficiency syndrome
(-related complex, oxime-substituted therapeutic compds. for diseases mediated by intracellular signaling)

IT Hepatitis
(alc., oxime-substituted therapeutic compds. for diseases mediated by intracellular signaling)

IT Inflammation inhibitors
(antiarthritics, oxime-substituted therapeutic compds. for diseases mediated by intracellular signaling)

IT Bronchodilators
(antiasthmatics, oxime-substituted therapeutic compds. for diseases mediated by intracellular signaling)

IT Antiarteriosclerotics
(antiatherosclerotics, oxime-substituted therapeutic compds. for diseases mediated by intracellular signaling)

IT Inflammation inhibitors
(antirheumatics, oxime-substituted therapeutic compds. for diseases mediated by intracellular signaling)

IT Thyroid gland, disease
(autoimmune thyroiditis, oxime-substituted therapeutic compds. for diseases mediated by intracellular signaling)

IT Adhesion
(bio-, oxime-substituted therapeutic compds. for diseases mediated by intracellular signaling)

IT Artery, disease
(coronary, oxime-substituted therapeutic compds. for diseases mediated by intracellular signaling)

IT Mental disorder
(dementia, HIV-assocd.; oxime-substituted therapeutic compds. for diseases mediated by intracellular signaling)

IT Periodontium
(disease, oxime-substituted therapeutic compds. for diseases mediated by intracellular signaling)

IT Connective tissue
(disease, scleroderma, oxime-substituted therapeutic compds. for diseases mediated by intracellular signaling)

IT Sleep
(disorder, oxime-substituted therapeutic compds. for diseases mediated by intracellular signaling)

IT Parturition
(disorder, premature, uterine infection-assocd.; oxime-substituted therapeutic compds. for diseases mediated by intracellular signaling)

IT Kidney, disease
(glomerulonephritis, oxime-substituted therapeutic compds. for diseases mediated by intracellular signaling)

IT Virus, animal
(human immunodeficiency, dementia; oxime-substituted therapeutic compds. for diseases mediated by intracellular signaling)

IT Intestine, disease
(inflammatory, oxime-substituted therapeutic compds. for diseases mediated by intracellular signaling)

IT Neoplasm inhibitors
(myelogenous leukemia, oxime-substituted therapeutic compds. for diseases mediated by intracellular signaling)

IT Heart, disease
(restenosis, oxime-substituted therapeutic compds. for diseases mediated by intracellular signaling)

IT Sepsis and Septicemia

(sepsis syndrome, oxime-substituted therapeutic compds. for diseases mediated by intracellular signaling)

IT Shock
(septic, oxime-substituted therapeutic compds. for diseases mediated by intracellular signaling)

IT Brain, disease
(stroke, oxime-substituted therapeutic compds. for diseases mediated by intracellular signaling)

IT 158327-67-4P 158327-72-1P 158327-73-2P 158327-75-4P 158327-94-7P
158327-95-8P
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(oxime-substituted therapeutic compds. for diseases mediated by intracellular signaling)

IT 83-67-0, Theobromine 109-70-6, 1-Bromo-3-chloropropane 111-87-5, Octanol, reactions 1010-59-9, Sodium theobromine 6294-17-3, 1-Bromo-6-chlorohexane 6493-05-6, Pentoxyfylline 7766-50-9, 10-Undecenyl bromide 39691-62-8, Nonylmagnesium bromide 67232-70-6
RL: RCT (Reactant)
(oxime-substituted therapeutic compds. for diseases mediated by intracellular signaling)

IT 35289-31-7P, 11-Dodecen-1-ol 71612-11-8P 156918-16-0P 156918-17-1P
156918-37-5P 156918-38-6P 156918-46-6P 156918-48-8P 156918-50-2P
156918-51-3P 156918-64-8P 156918-66-0P 158327-74-3P 158327-76-5P
158327-77-6P 158327-78-7P 158327-79-8P 158327-80-1P 158327-81-2P
158327-83-4P 158327-84-5P 158327-86-7P 158327-87-8P 158327-88-9P
158327-89-0P 158327-90-3P 158327-92-5P 158327-93-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(oxime-substituted therapeutic compds. for diseases mediated by intracellular signaling)

IT 158327-69-6P 158327-82-3P 158327-85-6P 158327-91-4P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(oxime-substituted therapeutic compds. for diseases mediated by intracellular signaling)

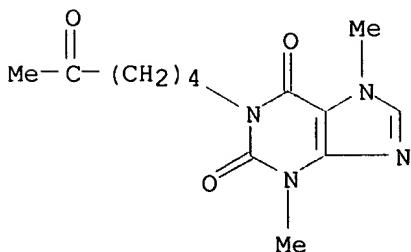
IT 158327-64-1 158327-66-3 158327-68-5 158327-70-9 158327-71-0
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(oxime-substituted therapeutic compds. for diseases mediated by intracellular signaling)

IT 158327-65-2
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(oxime-substituted therapeutic compds. for diseases mediated by intracellular signaling)

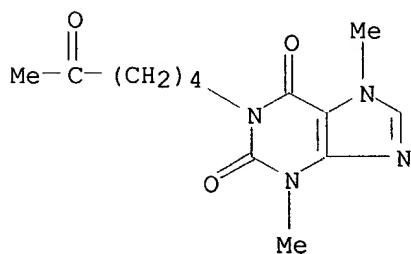
IT 6493-05-6, Pentoxyfylline
RL: RCT (Reactant)
(oxime-substituted therapeutic compds. for diseases mediated by intracellular signaling)

RN 6493-05-6 HCAPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-3,7-dimethyl-1-(5-oxohexyl)- (9CI) (CA INDEX NAME)



L63 ANSWER 18 OF 25 HCAPLUS COPYRIGHT 2002 ACS
 AN 1994:499228 HCAPLUS
 DN 121:99228
 TI Effect of pentoxifylline, a multidrug resistance reversal agent, on hemopoietic stem cell homing.
 AU Gude, R. P.; Chitnis, M. P.; Rao, S. G. A.
 CS Chemother. and Stem Cell Biol. Div., Cancer Res. Inst. Dr. E. Borges Marg, Bombay, India
 SO Cell Biol. Int. (1994), 18(2), 79-84
 CODEN: CBIIEV; ISSN: 1065-6995
 DT Journal
 LA English
 CC 1-6 (Pharmacology)
 AB This paper investigates the mechanism of mouse hemopoietic stem cell homing in mouse bone marrow. Pentoxifylline was shown to inhibit stem cell homing. The inhibition was reversible after 6 h. The results obtained suggest that the hemopoietic stem cell homing receptor is anchored to cytoskeletal support intracellularly.
 ST pentoxifylline hemopoietic stem cell homing; bone marrow spleen stem cell pentoxifylline
 IT **Bone marrow**
 Spleen
 (pentoxifylline inhibition of hematopoietic stem cell homing in)
 IT Hematopoietic precursor cell
 (stem, pentoxifylline inhibition of homing of, in bone marrow and spleen)
 IT 6493-05-6, Pentoxifylline
 RL: BIOL (Biological study)
 (hemopoietic stem cell homing in bone marrow and spleen inhibition by, as multidrug resistance reversal agent)
 IT 6493-05-6, Pentoxifylline
 RL: BIOL (Biological study)
 (hemopoietic stem cell homing in bone marrow and spleen inhibition by, as multidrug resistance reversal agent)
 RN 6493-05-6 HCAPLUS
 CN 1H-Purine-2,6-dione, 3,7-dihydro-3,7-dimethyl-1-(5-oxohexyl)- (9CI) (CA INDEX NAME)



L63 ANSWER 19 OF 25 HCAPLUS COPYRIGHT 2002 ACS
 AN 1993:109732 HCAPLUS
 DN 118:109732
 TI Modulation of cellular response to external and internal stimuli with xanthine derivatives
 IN Bianco, James A.; Bursten, Stuart L.; Singer, Jack W.
 PA Fred Hutchinson Cancer Research Center, USA
 SO PCT Int. Appl., 79 pp.
 CODEN: PIXXD2
 DT Patent

LA English
 IC ICM A61K031-52
 CC 63-6 (Pharmaceuticals)

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9221344	A2	19921210	WO 1992-US4349	19920522 <--
	WO 9221344	A3	19931209		
	W: AT, AU, BB, BG, BR, CA, CH, CS, DE, DK, ES, FI, GB, HU, JP, KP, KR, LK, LU, MG, MN, MW, NL, NO, PL, RO, RU, SD, SE, US				
	RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GN, GR, IT, LU, MC, ML, MR, NL, SE, SN, TD, TG				
	AU 9222475	A1	19930108	AU 1992-22475	19920522 <--
	AU 664189	B2	19951109		
	EP 573617	A1	19931215	EP 1992-915059	19920522 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, MC, NL, SE				
	JP 07500085	T2	19950105	JP 1992-500483	19920522 <--
	EP 1214938	A2	20020619	EP 2001-126058	19920522 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC				
	IL 101982	A1	20000229	IL 1992-101982	19920524 <--
	ZA 9203808	A	19930127	ZA 1992-3808	19920525 <--
	US 5856115	A	19990105	US 1994-196878	19940214 <--
	US 5585380	A	19961217	US 1995-378109	19950125 <--
PRAI	US 1991-704992	A	19910524	<--	
	US 1991-732227	A2	19910716	<--	
	EP 1992-915059	A3	19920522	<--	
	WO 1992-US4349	A	19920522	<--	
	US 1992-888722	B1	19920526	<--	
	US 1993-155361	B1	19931122	<--	

AB Xanthine derivs. (Markush structures given) are useful in modulating the effects of internal and external stimuli on cells by reversing the effects of these stimuli on the short-term secondary messenger pathways. In particular, the xanthines lower elevated levels of unsatd., nonarachidonate phosphatidic acid and diacylglycerol derived from the phosphatidic acid within seconds of the primary stimulus and their contact with the cells. The modulatory effect depends on the nature of the target cell and the stimulus applied. Effects of pentoxyphylline on the mesangial cell activation, **malignant** transformation of cells, cellular behavior, homeostasis are demonstrated.

ST xanthine cell response modulator; pentoxyphylline cell stimulus response modulation

IT Antigens

RL: BIOL (Biological study)
 (T-cell activation by, xanthine derivs. effect on)

IT Macrophage

Monocyte
 (activation by endotoxins in, xanthine derivs. effect on)

IT Hematopoietic precursor cell

(activation by **tumor** necrosis factor in, xanthine derivs. effect on)

IT Neoplasm

(cell activation by oncogenes in, xanthine derivs. effect on)

IT Mesenchyme

(cell activation by **tumor** necrosis factor in, xanthine derivs. effect on)

IT Blood platelet

Erythrocyte
 (from hematopoietic stem cell, xanthine derivs. effect on)

IT Phosphatidic acids

RL: BIOL (Biological study)
 (of animal cells, xanthine derivs. effect on)

IT Animal growth regulators

RL: BIOL (Biological study)

(smooth muscle cell activation by, xanthine derivs. effect on)

IT Hypertension
(xanthine derivs. effect on)

IT Lymphocyte
(B-cell, activation by antigens in, xanthine derivs. effect on)

IT Lymphocyte
(T-cell, activation by antigens in, xanthine derivs. effect on)

IT Therapeutics
(chemo-, hematopoietic stem cell activation by, xanthine derivs. effect on)

IT Toxins
RL: BIOL (Biological study)
(endo-, monocyte and macrophage activation by, xanthine derivs. effect on)

IT Artery
(endothelium, activation by hypertension-inducing substances in, xanthine derivs. effect on)

IT Kidney
(glomerulus, epithelial cell activation by interleukin-1 in, xanthine derivs. effect on)

IT Hematopoietic precursor cell
(granulocytic, from hematopoietic, xanthine derivs. effect on)

IT Hemopoietins
RL: FORM (Formation, nonpreparative)
(hematopoietic cell growth factors KL, formation of, in **bone** marrow stromal cells, xanthine derivs. effect on)

IT Virus, animal
(human immunodeficiency, T-cell activation by, xanthine derivs. effect on)

IT Lymphokines and Cytokines
RL: BIOL (Biological study)
(interleukin 1, kidney mesangial cell activation by, xanthine derivs. effect on)

IT Lymphokines and Cytokines
RL: FORM (Formation, nonpreparative)
(interleukin 6, formation of, in **bone** marrow stromal cells, xanthine derivs. effect on)

IT Kidney
(mesangium, activation by interleukin 1 in, xanthine derivs. effect on)

IT Gene, animal
RL: BIOL (Biological study)
(onco-, **neoplasm** cell activation by, xanthine derivs. effect on)

IT Muscle
(smooth, cell activation by growth factors in, xanthine derivs. effect on)

IT Hematopoietic precursor cell
(stem, activation by chemotherapeutic agents in, xanthine derivs. effect on)

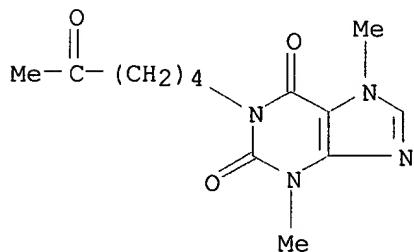
IT **Bone marrow**
(stroma, activation by **tumor** necrosis factor in, xanthine derivs. effect on)

IT Lymphokines and Cytokines
RL: BIOL (Biological study)
(**tumor** necrosis factor, mesenchymal cell activation by, xanthine derivs. effect on)

IT 9025-77-8, Phosphatidic acid phosphohydrolase 9081-03-2
RL: PRP (Properties)
(activity of, xanthine derivs. effect on)

IT 6493-05-6, Pentoxifylline 6493-06-7, 1-(5-Hydroxyhexyl)-3,7-dimethylxanthine 107767-63-5, 1-(5-Methyl-5-hydroxyhexyl)-3,7-dimethylxanthine
RL: BIOL (Biological study)

(cellular response to internal and external stimuli modulation by)
 IT 81669-70-7, Metalloprotease
 RL: FORM (Formation, nonpreparative)
 (formation of, by glomerular epithelial cells, xanthine derivs. effect on)
 IT 106956-32-5, Oncostatin-M 143011-72-7, G-CSF
 RL: FORM (Formation, nonpreparative)
 (formation of, in bone marrow stromal cells, xanthine derivs. effect on)
 IT 9035-51-2, P 450, biological studies
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (inhibitors, xanthine derivs. as)
 IT 83869-56-1, GM-CSF
 RL: BIOL (Biological study)
 (monocyte and macrophage activation by, xanthine derivs. effect on)
 IT 6493-05-6, Pentoxifylline
 RL: BIOL (Biological study)
 (cellular response to internal and external stimuli modulation by)
 RN 6493-05-6 HCPLUS
 CN 1H-Purine-2,6-dione, 3,7-dihydro-3,7-dimethyl-1-(5-oxohexyl)- (9CI) (CA INDEX NAME)



L63 ANSWER 20 OF 25 HCPLUS COPYRIGHT 2002 ACS
 AN 1992:99328 HCPLUS
 DN 116:99328
 TI Method for treating equine navicular disease with pentoxifylline, and composition containing pentoxifylline for administrating to horses
 IN Drizen, Alan
 PA Hyal Pharmaceutical Corp., Can.
 SO U.S., 9 pp.
 CODEN: USXXAM
 DT Patent
 LA English
 IC ICM A01N043-90
 NCL 514261000
 CC 1-8 (Pharmacology)
 Section cross-reference(s): 63
 FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
-----	-----	-----	-----	-----
PI US 5077296	A	19911231	US 1987-128175	19871203 <--
AB	Equine navicular disease is treated with a compn. contg. pentoxifylline (I) in a daily dose of 6-30 g to alleviate lameness. Preferably the compn. comprises I 7.2, confectioners' sugar 8.5, corn sugar 83.895, colloidal SiO ₂ 0.247, and artificial color 0.158 wt.%. Horses were treated orally with I.			
ST	horse navicular bone disease pentoxifylline			
IT	Horse (navicular disease treatment in, pentoxifylline for)			
IT	Pharmaceutical dosage forms			

(of pentoxifylline, for navicular disease treatment in horse)

IT **Bone**
 (navicular, treatment of, of horse, with pentoxifylline)

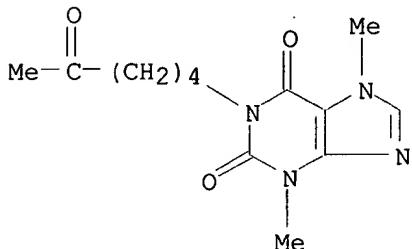
IT Pharmaceutical dosage forms
 (oral, of pentoxifylline, for navicular disease treatment in horse)

IT 6493-05-6, Pentoxifylline
 RL: BIOL (Biological study)
 (navicular disease in horse treatment with)

IT 6493-05-6, Pentoxifylline
 RL: BIOL (Biological study)
 (navicular disease in horse treatment with)

RN 6493-05-6 HCPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-3,7-dimethyl-1-(5-oxohexyl)- (9CI) (CA INDEX NAME)



L63 ANSWER 21 OF 25 HCPLUS COPYRIGHT 2002 ACS
 AN 1991:441508 HCPLUS
 DN 115:41508
 TI Fluosol-DA/carbogen with lonidamine or pentoxifylline as modulators of alkylating agents in the FSaIIC fibrosarcoma
 AU Teicher, Beverly A.; Herman, Terence S.; Tanaka, Juichi; Dezube, Bruce; Pardee, Arthur; Frei, Emil, III
 CS Dana-Farber Cancer Inst., Boston, MA, 02115, USA
 SO Cancer Chemother. Pharmacol. (1991), 28(1), 45-50
 CODEN: CCPHDZ; ISSN: 0344-5704
 DT Journal
 LA English
 CC 1-6 (Pharmacology)
 AB In an effort to increase the efficacy of several **antineoplastic** alkylating agents (CDDP, L-PAM, CTX, or BCNU), the authors examd. the effect of the modulator Fluosol-DA/carbogen in combination with a second modulator, either lonidamine or pentoxifylline, on the survival of FSaIIC **tumor** cells and of **bone** marrow CFU-GM from **tumor** -bearing C3H mice. Fluosol-DA/carbogen increased the **tumor**-cell killing activity of each alkylating agent by about 10 times. In contrast, lonidamine alone did not significantly increase the cytoidal activity of any of the alkylating agents tested. However, in combination with Fluosol-DA/carbogen, the use of lonidamine produced about a 100-fold increase in the **tumor** cell kill achieved with CDDP as compared with CDDP alone. No increase in **tumor** cell kill over that produced with the single modulator Fluosol-DA/carbogen was seen following the addn. of lonidamine to the combination treatment with L-PAM, CTX, or BCNU. Unfortunately, although neither lonidamine nor Fluosol-DA/carbogen alone significantly increased alkylator toxicity to **bone** marrow CFU-GM, the combination of modulators increased the toxicity of each alkylating agent to **bone** marrow by about 10 times. Pentoxifylline caused an increase in alkylator activity against the FSaIIC fibrosarcoma only when used with BCNU; this effect was further augmented by the addn. of Fluosol-DA/carbogen. The combination of modulators pentoxifylline plus Fluosol-DA/carbogen was more effective than

Fluosol-DA/carbogen alone only when the former was used with BCNU, whereas only minimal increases in **tumor**-cell killing activity were obtained with this modulator combination and CDDP, L-PAM, or CTX. Pentoxifylline increased the **bone** marrow CFU-GM toxicity of L-PAM by about 10 times. The **bone** marrow CFU-GM toxicity was further increased by Fluosol-DA/carbogen, as was the toxicity of each of the other alkylating agents. Lonidamine plus Fluosol-DA/carbogen may be useful in increasing the therapeutic efficacy of CDDP, and the combination of pentoxifylline plus Fluosol-DA/carbogen might improve the **antitumor** activity of BCNU.

ST Fluosol DA carbogen alkylating **antitumor** modulator; lonidamine carbogen alkylating **antitumor** modulator; pentoxifylline Fluosol DA alkylating **antitumor** modulator

IT **Bone marrow, toxic chemical and physical damage**
(alkylating agents toxicity to, Fluosol-DA/carbogen with lonidamine or pentoxifylline effect on)

IT **Neoplasm inhibitors**
(alkylating agents, **antitumor** activity and **bone** marrow CFU-GM toxicity of, Fluosol-DA and carbogen effect on)

IT Hematopoietic precursor cell
(granulocyte-macrophage colony-forming, alkylating agents toxicity to, Fluosol-DA/carbogen with lonidamine or pentoxifylline effect on)

IT 8063-77-2, Carbogen
RL: BIOL (Biological study)
(alkylating agents **antitumor** activity and **bone** marrow CFU-GM toxicity response to Fluosol-DA and)

IT 6493-05-6, Pentoxifylline 50264-69-2, Lonidamine
RL: BIOL (Biological study)
(alkylating agents **antitumor** activity and **bone** marrow CFU-GM toxicity response to Fluosol-DA and carbogen and)

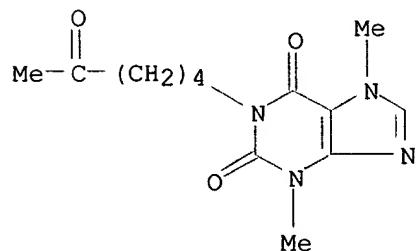
IT 75216-20-5, Fluosol-DA
RL: BIOL (Biological study)
(alkylating agents **antitumor** activity and **bone** marrow CFU-GM toxicity response to carbogen and)

IT 50-18-0, Cyclophosphamide 148-82-3, Melphalan 154-93-8, BCNU
15663-27-1, Cisplatin
RL: BIOL (Biological study)
(**antitumor** activity and **bone** marrow CFU-GM toxicity of, Fluosol-DA and carbogen effect on)

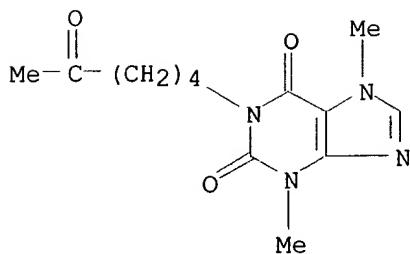
IT 6493-05-6, Pentoxifylline
RL: BIOL (Biological study)
(alkylating agents **antitumor** activity and **bone** marrow CFU-GM toxicity response to Fluosol-DA and carbogen and)

RN 6493-05-6 HCPLUS

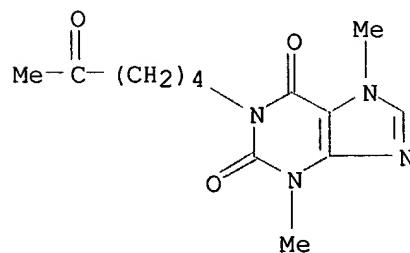
CN 1H-Purine-2,6-dione, 3,7-dihydro-3,7-dimethyl-1-(5-oxohexyl)- (9CI) (CA INDEX NAME)



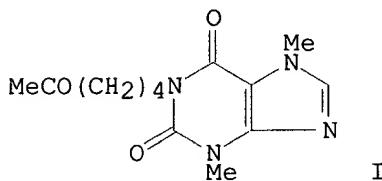
TI DNA repair and drug resistance. Enhancement of the effects of **anticancer** agents by DNA repair inhibitors
 AU Tomita, Katsuro; Tsuchiya, Hiroyuki; Sasaki, Takuma
 CS Sch. Med., Kanazawa Univ., Kanazawa, Japan
 SO Gan to Kagaku Ryoho (1989), 16(3, Pt. 2), 576-84
 CODEN: GTKRDX; ISSN: 0385-0684
 DT Journal
 LA Japanese
 CC 1-6 (Pharmacology)
 AB Recently, it has been revealed that **anticancer** effects are increased by inhibition of DNA repair of **cancer** cells. Methylxanthines block DNA repair. The combined effects of CDDP and caffeine or pentoxyphylline were studied by using human **osteosarcoma** cells (OST strain). When 2 mM caffeine was added before 1 h exposure of CDDP or caffeine and CDDP was added simultaneously for 1 h, no synergistic effect was shown. On the other hand, marked synergistic growth inhibition was obsd. when caffeine or pentoxyphylline was added continuously after 1 h exposure of CDDP. The addn. of caffeine from 24 to 48 h after 1 h exposure of CDDP also showed synergistic effects as the doubling time of OST cells was about 30 h. Three patients with advanced **osteosarcomas** were treated with the combination of CDDP, ADM (adriamycin), and caffeine or that of CDDP and caffeine. A 9-yr-old boy with multicentric **osteosarcoma** treated by the combination of CDDP, ADM, and caffeine showed partial response, and caffeine did not increase the side effects of **anticancer** agents. Hence the study on overcoming drug resistance by the inhibition of DNA repair will be promising.
 ST **antitumor** resistance methylxanthine DNA repair inhibitor
 IT Deoxyribonucleic acid repair
 (inhibitors, methylxanthines as, **antitumor** drug resistance inhibition by)
 IT Drug resistance
 (of **osteosarcoma** to **antitumor** agents, methylxanthine DNA-repair inhibitors inhibition of, in humans)
 IT Neoplasm inhibitors
 (**osteosarcoma**, resistance to, methylxanthine DNA-repair inhibitors decrease of, in humans)
 IT 15663-27-1, CDDP 23214-92-8, Adriamycin
 RL: BIOL (Biological study)
 (**osteosarcoma** inhibition by, DNA repair inhibitors methylxanthines enhancement of, drug resistance inhibition in, in humans)
 IT 58-08-2, Caffeine, biological studies 58-55-9, Theophylline, biological studies 6493-05-6, Pentoxyphylline 28109-92-4D, Methylxanthine, derivs.
 RL: BIOL (Biological study)
 (**osteosarcoma** resistance to **antitumor** agents inhibition by, in humans)
 IT 6493-05-6, Pentoxyphylline
 RL: BIOL (Biological study)
 (**osteosarcoma** resistance to **antitumor** agents inhibition by, in humans)
 RN 6493-05-6 HCAPLUS
 CN 1H-Purine-2,6-dione, 3,7-dihydro-3,7-dimethyl-1-(5-oxohexyl)- (9CI) (CA INDEX NAME)



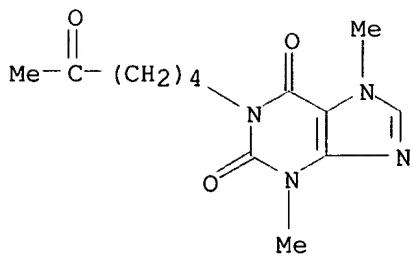
L63 ANSWER 23 OF 25 HCAPLUS COPYRIGHT 2002 ACS
 AN 1985:125570 HCAPLUS
 DN 102:125570
 TI Study of antiosteoporotic agents in tissue culture
 AU Robin, J. C.; Ambrus, J. L.
 CS Roswell Park Mem. Inst., Buffalo, NY, 14263, USA
 SO J. Med. (Westbury, N. Y.) (1984), 15(4), 319-22
 CODEN: JNMDBO; ISSN: 0025-7850
 DT Journal
 LA English
 CC 1-12 (Pharmacology)
 AB Cultures of **osteoblast**-like cells were established from calvariae of Sprague-Dawley rats. Pentoxyphylline [6493-05-6] increased cAMP [60-92-4] levels and Ca uptake in these cultures. However, Ca uptake increased at lower levels than required to increase cAMP levels. Apparently, mechanisms unrelated to cAMP are also involved in these phenomena.
 ST **osteoporosis** inhibitor evaluation cell culture; pentoxyphylline .
osteoporosis cell culture
 IT **Osteoporosis**
 (inhibition of, by pentoxyphylline, tissue culture method for detn. of)
 IT Animal tissue culture
 (of **bone**, **osteoporosis** inhibition by pentoxyphylline
 in)
 IT 60-92-4 7440-70-2, biological studies
 RL: BIOL (Biological study)
 (of **bone**, **osteoporosis** inhibition by pentoxyphylline
 in relation to)
 IT 6493-05-6
 RL: BIOL (Biological study)
 (**osteoporosis** inhibition by, culture method for detn. of)
 IT 6493-05-6
 RL: BIOL (Biological study)
 (**osteoporosis** inhibition by, culture method for detn. of)
 RN 6493-05-6 HCAPLUS
 CN 1H-Purine-2,6-dione, 3,7-dihydro-3,7-dimethyl-1-(5-oxohexyl)- (9CI) (CA INDEX NAME)



L63 ANSWER 24 OF 25 HCAPLUS COPYRIGHT 2002 ACS
 AN 1983:516034 HCAPLUS
 DN 99:116034
 TI Studies on **osteoporoses**. XI. Effects of a methylxanthine derivative
 AU Robin, John C.; Ambrus, Julian L.
 CS Roswell Park Mem. Inst., Buffalo, NY, 14263, USA
 SO J. Med. (Westbury, N. Y.) (1983), 14(2), 137-45
 CODEN: JNMDBO; ISSN: 0025-7850
 DT Journal
 LA English
 CC 1-12 (Pharmacology)
 Section cross-reference(s): 14
 GI



AB Pentoxifylline (I) [6493-05-6] (12 mg/kg i.m. twice daily) prevented exptl. **osteoporosis** in mice. Pentoxifylline (0.1-100 μ g/mL) increased Ca^{2+} uptake and cAMP [60-92-4] prodn. in **osteoblast**-like **bone** cells isolated from fetal Sprague-Dawley rats. Theor. implications for **osteoblast** control of **bone** resorption are discussed.
 ST pentoxifylline **osteoporosis**
 IT **Osteoporosis**
 (pentoxifylline prevention of, calcium uptake and cyclic AMP formation in **bone** cells in relation to)
 IT 60-92-4
 RL: FORM (Formation, nonpreparative)
 (formation of, in **bone** cells, pentoxifylline effect on, **osteoporosis** in relation to)
 IT 6493-05-6
 RL: BIOL (Biological study)
 (**osteoporosis** prevention by, calcium uptake and cyclic AMP formation in **bone** cells in relation to)
 IT 7440-70-2, biological studies
 RL: BIOL (Biological study)
 (uptake of, by **bone** cells, pentoxifylline effect on, **osteoporosis** in relation to)
 IT 6493-05-6
 RL: BIOL (Biological study)
 (**osteoporosis** prevention by, calcium uptake and cyclic AMP formation in **bone** cells in relation to)
 RN 6493-05-6 HCAPLUS
 CN 1H-Purine-2,6-dione, 3,7-dihydro-3,7-dimethyl-1-(5-oxohexyl)- (9CI) (CA INDEX NAME)



L63 ANSWER 25 OF 25 HCPLUS COPYRIGHT 2002 ACS

AN 1980:69360 HCPLUS

DN 92:69360

TI The effects of trental, levamisole and some other cyclic nucleotides on the proliferation of stem **bone** marrow cells (KOE)

AU Fedorov, N. A.; Ermil'chenko, G. V.; Koreshkova, N. A.; Stepanova, S. B.

CS Lab. Biochem., Cent. Inst. Haematol. Blood Transfus., Moscow, 125167, USSR

SO Adv. Biosci. (1979), Volume Date 1978, 24(Cyclic Nucleotides

Ther. Perspect.), 217-23

CODEN: AVBIB9; ISSN: 0065-3446

DT Journal

LA English

CC 1-4 (Pharmacodynamics)

AB The proliferation of mouse **bone** marrow stem cells was increased by 2-h incubation with trental [6493-05-6] (10-3M), levamisole [14769-73-4] (2.5 .times. 10-6M), 1-(N-chloroacetylaminoethoxy)cyclic AMP [71240-57-8] (10-8M), 8-(N-chloroacetylaminoethylamino) cyclic AMP [65259-74-7] (10-8M), or 1-[N-(fluorosulfonyl)benzoylaminoethoxy] cyclic AMP [71262-88-9] (10-8M).

ST **bone** marrow proliferation drug; stem cell proliferation drug; trental **bone** marrow proliferation; levamisole **bone** marrow proliferation; cyclic AMP deriv **bone** marrow

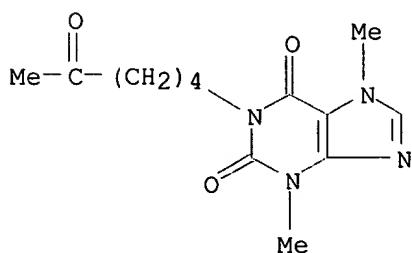
IT **Bone** marrow
(stem cell, cyclic nucleotides and levamisole and trental stimulation of proliferation of)

IT 6493-05-6 14769-73-4 65259-74-7 71240-57-8 71262-88-9
RL: BIOL (Biological study)
(**bone** marrow stem cell proliferation stimulation by)

IT 6493-05-6
RL: BIOL (Biological study)
(**bone** marrow stem cell proliferation stimulation by)

RN 6493-05-6 HCPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-3,7-dimethyl-1-(5-oxohexyl)- (9CI) (CA INDEX NAME)



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FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 31 July 2002 (20020731/ED)

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L83 ANSWER 1 OF 3 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

AN 1996:273382 BIOSIS

DN PREV199698829511

TI Suppressive effect of N-(benzyloxycarbonyl)-L-phenylalanyl-L-tyrosinal on
bone resorption in vitro and in vivo.

AU Woo, Je-Tae; Yamaguchi, Kohji; Hayama, Takahiro; Kobori, Takeo; Sigeizumi, Sanae; Sugimoto, Kikuo; Kondo, Kiyosi; Tsuji, Tomoko (1); Ohba, Yasuo; Tagami, Kahori; Sumitani, Koji

CS (1) Sagami Chem. Res. Cent., Nishioonuma 4-4-1, Sagamihara, Kanagawa 229 Japan

SO European Journal of Pharmacology, (1996) Vol. 300, No. 1-2, pp. 131-135.
ISSN: 0014-2999.

DT Article

LA English

AB The suppressive effect of N-(benzyloxycarbonyl)-L-phenylalanyl-L-tyrosinal on **bone resorption** was examined in vitro and in vivo.

This synthetic **peptidyl aldehyde** was found to be a potent and selective cathepsin L inhibitor in our screening for cysteine protease inhibitors. In the pit formation assay with unfractionated rat bone cells, 1.5 nM of this compound markedly inhibited parathyroid hormone-stimulated osteoclastic **bone resorption**. In addition, intraperitoneal administration of this **peptidyl aldehyde** (2.5-10 mg/kg) for 4 weeks suppressed bone weight loss dose dependently in the ovariectomized mouse, experimental model of osteoporosis. Hydroxyproline measurement of the decalcified femurs from these ovariectomized mice suggested that this compound acts as a **bone resorption** suppressor through the inhibition of collagen degradation.

CC Cytology and Cytochemistry - Animal *02506

Biochemical Methods - Proteins, Peptides and Amino Acids *10054

Biochemical Studies - General 10060

Biochemical Studies - Proteins, Peptides and Amino Acids 10064

Biochemical Studies - Minerals 10069

Enzymes - Methods *10804

Enzymes - Physiological Studies *10808

Pathology, General and Miscellaneous - Therapy *12512

Metabolism - Minerals *13010

Metabolism - Proteins, Peptides and Amino Acids *13012

Bones, Joints, Fasciae, Connective and Adipose Tissue - Anatomy

*18002

Bones, Joints, Fasciae, Connective and Adipose Tissue - Physiology and Biochemistry *18004

Bones, Joints, Fasciae, Connective and Adipose Tissue - Pathology *18006

Pharmacology - General *22002

Pharmacology - Drug Metabolism; Metabolic Stimulators *22003

Pharmacology - Clinical Pharmacology 22005

Pharmacology - Connective Tissue, Bone and Collagen - Acting Drugs *22012

Developmental Biology - Embryology - Morphogenesis, General *25508

BC In Vitro Studies, Cellular and Subcellular *32600
 BC Muridae *86375
 IT Major Concepts
 Cell Biology; Development; Enzymology (Biochemistry and Molecular Biophysics); Metabolism; Methods and Techniques; Pathology; Pharmacology; Skeletal System (Movement and Support)
 IT Chemicals & Biochemicals
 CATHEPSIN L; CYSTEINE PROTEASE
 IT Miscellaneous Descriptors
 CATHEPSIN L; COLLAGEN DEGRADATION INHIBITION; CYSTEINE PROTEASE INHIBITOR; DIPEPTIDYL ALDEHYDE; ENZYME INHIBITOR-DRUG; EXPERIMENTAL OSTEOPOROSIS MODEL; IN-VITRO; IN-VIVO; METABOLIC-DRUG; N-(BENZYLOXYCARBONYL)-L-PHENYLALANYL-L-TYROSINAL; OSTEOPOROTIC DRUG CANDIDATE; PHARMACODYNAMICS
 ORGN Super Taxa
 Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia
 ORGN Organism Name
 rat (Muridae)
 ORGN Organism Superterms
 animals; chordates; mammals; nonhuman mammals; nonhuman vertebrates; rodents; vertebrates
 RN 60616-82-2 (CATHEPSIN L)
 37353-41-6 (CYSTEINE PROTEASE)
 L83 ANSWER 2 OF 3 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
 AN 1985:93919 BIOSIS
 DN BR28:93919
 TI STUDY OF ANTIOSSTEOPOROTIC AGENTS IN TISSUE CULTURE.
 AU ROBIN J C; AMBRUS J L
 CS ROSWELL PARK MEMORIAL INST., BUFFALO, NY 14263.
 SO J. Med. (Westbury, N. Y.), (1984 (RECD 1985)) 15 (4), 319-322.
 CODEN: JNMDBO. ISSN: 0025-7850.
 FS BR; OLD
 LA English
 CC Biochemical Studies - General 10060
 Biochemical Studies - Nucleic Acids, Purines and Pyrimidines 10062
 Metabolism - Nucleic Acids, Purines and Pyrimidines *13014
 Bones, Joints, Fasciae, Connective and Adipose Tissue - General;
 Methods *18001
 Pharmacology - Drug Metabolism; Metabolic Stimulators *22003
 Pharmacology - Connective Tissue, Bone and Collagen - Acting Drugs *22012
 BC Tissue Culture, Apparatus, Methods and Media 32500
 BC Muridae 86375
 IT Miscellaneous Descriptors
 RAT PENTOXIFYLLINE METABOLIC-DRUG CYCLIC AMP
 RN 60-92-4 (CYCLIC AMP)
 6493-05-6 (PENTOXIFYLLINE)
 L83 ANSWER 3 OF 3 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
 AN 1984:172630 BIOSIS
 DN BA77:5614
 TI STUDIES ON OSTEO POROSSES 11. EFFECTS OF A METHYL XANTHINE DERIVATIVE A PRELIMINARY REPORT.
 AU ROBIN J C; AMBRUS J L
 CS ROSWELL PARK MEMORIAL INST., BUFFALO, N.Y. 14263.
 SO J MED (WESTBURY), (1983) 14 (2), 137-146.
 CODEN: JNMDBO. ISSN: 0025-7850.
 FS BA; OLD
 LA English
 AB Heparin (500 U/kg s.c. BID [twice a day]) induced significant osteoporosis in C3H/St(Ha) female mice after 3 mo. treatment. Pentoxyfylline (12 mg/kg i.m. BID) prevented this experimental osteoporosis. Osteoporosis

was measured by in vivo neutron activation analysis and results were confirmed by atomic absorption spectroscopy. **Pentoxifylline** (0.1-100 .mu.g/ml) increased Ca uptake and cAMP production in osteoblast-like bone cells isolated from fetal Sprague-Dawley rats. Theoretical implications for osteoblast control of bone resorption are discussed.

CC Cytology and Cytochemistry - Animal 02506
 Biochemical Studies - General 10060
 Biochemical Studies - Nucleic Acids, Purines and Pyrimidines 10062
 Biochemical Studies - Carbohydrates 10068
 Biochemical Studies - Minerals 10069
 Biophysics - General Biophysical Studies 10502
 Biophysics - General Biophysical Techniques 10504
 Metabolism - Minerals *13010
 Metabolism - Nucleic Acids, Purines and Pyrimidines 13014
 Muscle - General; Methods 17501
Bones, Joints, Fasciae, Connective and Adipose Tissue - Pathology
 *18006
 Integumentary System - General; Methods 18501
Pharmacology - Connective Tissue, Bone and Collagen - Acting Drugs
 *22012
 Routes of Immunization, Infection and Therapy 22100
 Toxicology - General; Methods and Experimental 22501
 Toxicology - Pharmacological Toxicology *22504
 Developmental Biology - Embryology - General and Descriptive 25502
 BC Muridae 86375
 IT Miscellaneous Descriptors
 MOUSE RAT PENTOXIFYLLINE METABOLIC-DRUG CYCLIC AMP CALCIUM
 UPTAKE HEPARIN INDUCED
 RN 60-92-4 (CYCLIC AMP)
 6493-05-6 (PENTOXIFYLLINE)
 7440-70-2 (CALCIUM)
 9005-49-6 (HEPARIN)
 28109-92-4D (METHYL XANTHINE)

=> fil medline
 FILE 'MEDLINE' ENTERED AT 15:55:16 ON 05 AUG 2002

FILE LAST UPDATED: 3 AUG 2002 (20020803/UP). FILE COVERS 1958 TO DATE.

On June 9, 2002, MEDLINE was reloaded. See HELP RLOAD for details.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2002 vocabulary. Enter HELP THESAURUS for details.

THIS FILE CONTAINS CAS REGISTRY NUMBERS FOR EASY AND ACCURATE SUBSTANCE IDENTIFICATION.

=> d 1110 all tot

L110 ANSWER 1 OF 7 MEDLINE
 AN 97406728 MEDLINE
 DN 97406728 PubMed ID: 9260111
 TI Tumor necrosis factor-alpha and interleukin-6 release from white blood cells induced by different graft materials in vitro are affected by **pentoxifylline** and iloprost.
 AU Swartbol P; Truedsson L; Parsson H; Norgren L
 CS Department of Surgery, Lund University, Sweden.
 SO JOURNAL OF BIOMEDICAL MATERIALS RESEARCH, (1997 Sep 5) 36 (3)
 400-6.
 Journal code: 0112726. ISSN: 0021-9304.
 CY United States

DT Journal; Article; (JOURNAL ARTICLE)
 LA English
 FS Priority Journals
 EM 199709
 ED Entered STN: 19971008
 Last Updated on STN: 19971008
 Entered Medline: 19970923
 AB Inflammatory mediators such as cytokines produced by white blood cells (WBCs) at the site of implantation are important for the biocompatibility of vascular grafts. The aim of the present study was to demonstrate the tumor necrosis factor-alpha (TNF-alpha) and interleukin-6 (IL-6) release from WBCs incubated with expanded polytetrafluoroethylene (ePTFE) or woven Dacron grafts. In a second series the effects of **pentoxifylline** (PTX) and iloprost (ILO), both known to inhibit white blood cell function, on this release were determined. Woven Dacron grafts induced significantly higher release of both TNF-alpha and IL-6 compared to ePTFE. TNF-alpha was detectable first after 2 h, whereas IL-6 was seen after 4 h. Maximum values were reached at 6 and 12 h, respectively. The addition of an endotoxin gave more pronounced patterns of cytokine release not influenced by time. Preincubation with both PTX and ILO at final concentrations of 100 and 10 micrograms/mL, respectively, reduced significantly the TNF-alpha release without differences between the two graft materials, whereas the effect on the IL-6 release varied and was graft material-dependent. In conclusion, graft material-dependent induction of TNF-alpha and IL-6 from WBCs was demonstrated. PTX and ILO influenced the cytokine release. It might be suggested that graft material-induced cytokine production could contribute to intimal hyperplasia in vivo. The present findings encourage further studies regarding graft material-induced WBC alterations and the role of pharmacologic agents influencing this function.
 CT Check Tags: Human; Support, Non-U.S. Gov't
 *Biocompatible Materials: AE, adverse effects
 ***Bioprosthetic**: AE, adverse effects
 *Iloprost
 *Interleukin-6: SE, secretion
 *Leukocytes: DE, drug effects
 .Leukocytes: ME, metabolism
 ***Pentoxifylline**
 *Tumor Necrosis Factor: SE, secretion
 RN 6493-05-6 (**Pentoxifylline**): 78919-13-8 (Iloprost)
 CN 0 (Biocompatible Materials); 0 (Interleukin-6); 0 (Tumor Necrosis Factor)
 L110 ANSWER 2 OF 7 MEDLINE
 AN 94055565 MEDLINE
 DN 94055565 PubMed ID: 8237250
 TI **Pentoxifylline** inhibits the proliferation and glycosaminoglycan synthesis of cultured fibroblasts derived from patients with Graves' ophthalmopathy and pretibial myxoedema.
 AU Chang C C; Chang T C; Kao S C; Kuo Y F; Chien L F
 CS Department of Dermatology, College of Medicine, National Taiwan University, Taipei, Republic of China.
 SO ACTA ENDOCRINOLOGICA, (1993 Oct) 129 (4) 322-7.
 Journal code: 0370312. ISSN: 0001-5598.
 CY Denmark
 DT Journal; Article; (JOURNAL ARTICLE)
 LA English
 FS Priority Journals
 EM 199312
 ED Entered STN: 19940117
 Last Updated on STN: 19940117
 Entered Medline: 19931217
 AB Excessive amounts of glycosaminoglycans accumulate in the extraocular muscles of patients with Graves' ophthalmopathy and in the affected skin

of patients with pretibial myxoedema. It is widely accepted that fibroblasts are the sources of glycosaminoglycan synthesis. **Pentoxifylline**, an analogue of the methylxanthine theobromine, inhibits the proliferation and certain biosynthetic activities of fibroblasts derived from normal human skin and from skin of patients with some fibrotic disorders. Our objective was to determine whether **pentoxifylline** has similar effects on fibroblasts derived from patients with Graves' ophthalmopathy and pretibial myxoedema and could serve as a candidate for the treatment of these manifestations. Fibroblasts from the extraocular muscles of two patients with Graves' ophthalmopathy and normal extraocular muscles of two subjects with strabismus, as well as the affected skin of two patients with pretibial myxoedema were cultured in vitro in the presence and absence of **pentoxifylline** to assay its effect on the proliferation of fibroblasts and their production of glycosaminoglycans. In subconfluent fibroblast cultures, **pentoxifylline** treatment caused a dose-dependent inhibition of serum-driven fibroblast proliferation. In confluent fibroblast cultures both in the presence and absence of serum, exposure to **pentoxifylline** similarly resulted in a dose-dependent inhibition of glycosaminoglycan synthesis for all these different kinds of fibroblasts. These findings may form the rationale for a clinical trial using **pentoxifylline** for the treatment of Graves' ophthalmopathy and pretibial myxoedema.

CT Check Tags: Female; Human; Male; Support, Non-U.S. Gov't

Adult

Cell Division: DE, drug effects

Cells, Cultured

Child, Preschool

*Fibroblasts: ME, metabolism

*Fibroblasts: PA, pathology

*Glycosaminoglycans: BI, biosynthesis

Graves' Disease: ME, metabolism

*Graves' Disease: PA, pathology

Middle Age

Myxedema: ME, metabolism

*Myxedema: PA, pathology

Oculomotor Muscles: ME, metabolism

Oculomotor Muscles: PA, pathology

***Pentoxifylline**: PD, pharmacology

Skin: ME, metabolism

Skin: PA, pathology

Tibia

RN 6493-05-6 (**Pentoxifylline**)

CN 0 (Glycosaminoglycans)

L110 ANSWER 3 OF 7 MEDLINE

AN 86202007 MEDLINE

DN 86202007 PubMed ID: 2939303

TI Trends in revascularization of the lower extremity.

AU Hallett J W Jr

SO MAYO CLINIC PROCEEDINGS, (1986 May) 61 (5) 369-76.

Journal code: 0405543. ISSN: 0025-6196.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Abridged Index Medicus Journals; Priority Journals

EM 198605

ED Entered STN: 19900321

Last Updated on STN: 19900321

Entered Medline: 19860528

AB Several trends are evident in revascularization of the lower extremity.

Currently, few patients with severe leg ischemia undergo amputation without prior surgical or angioplasty attempts at revascularization.

Percutaneous balloon angioplasty and thrombolytic therapy have had a definite but limited influence on the treatment of all patients with lower-limb arterial disease. Although **pentoxifylline**, a hemorrheologic agent, is being widely used, it has not changed the need for surgical intervention in patients with severe arterial disease. In the aggressive approach to save legs with severe popliteal-tibial disease, the use of femorotibial grafts is increasing. In situ saphenous vein grafting is becoming the operation of choice for infrapopliteal occlusive disease. For most patients with severe lower-extremity arterial occlusive disease, a properly selected and conducted operation remains the safest and most durable treatment.

CT Check Tags: Human
 Angioplasty, Balloon
 Aorta, Abdominal: SU, surgery
 Arterial Occlusive Diseases: DT, drug therapy
 Arterial Occlusive Diseases: RA, radiography
 *Arterial Occlusive Diseases: SU, surgery
 Femoral Artery: SU, surgery
 Iliac Artery: SU, surgery
 Lasers: TU, therapeutic use
 *Leg: BS, blood supply
Pentoxifylline: TU, therapeutic use
 Popliteal Artery: SU, surgery
 Subtraction Technique
Tibia: BS, blood supply
 Ultrasonography

RN 6493-05-6 (**Pentoxifylline**)

L110 ANSWER 4 OF 7 MEDLINE
 AN 86002672 MEDLINE
 DN 86002672 PubMed ID: 3899404
 TI Warfarin versus dipyridamole-aspirin and **pentoxifylline**-aspirin for the prevention of prosthetic heart valve thromboembolism: a prospective randomized clinical trial.
 AU Mok C K; Boey J; Wang R; Chan T K; Cheung K L; Lee P K; Chow J; Ng R P; Tse T F
 SO CIRCULATION, (1985 Nov) 72 (5) 1059-63.
 Journal code: 0147763. ISSN: 0009-7322.
 CY United States
 DT (CLINICAL TRIAL)
 Journal; Article; (JOURNAL ARTICLE)
 (RANDOMIZED CONTROLLED TRIAL)
 LA English
 FS Abridged Index Medicus Journals; Priority Journals
 EM 198511
 ED Entered STN: 19900321
 Last Updated on STN: 19950206
 Entered Medline: 19851121
 AB In a prospective, randomized, parallel study, two regimens of platelet-suppressant therapy (PST)--dipyridamole-aspirin and **pentoxifylline**-aspirin--were compared with standard oral anticoagulation with warfarin in the prevention of prosthetic heart valve thromboembolism. In the entire group of 254 patients followed for 395.6 patient-years, the thromboembolic rate was significantly less in the warfarin group (warfarin vs dipyridamole-aspirin, p less than .005; warfarin vs **pentoxifylline**-aspirin, p less than .05). Subgroup analysis disclosed that, in patients with isolated mitral valve replacement, warfarin was superior to both of the PSTs with respect to the prevention of thromboembolism (warfarin vs dipyridamole-aspirin, p = .005; warfarin vs **pentoxifylline**-aspirin, p less than .05). Furthermore, a significant number of our patients could not tolerate the antiplatelet agents. However, in the rare situation in which repeated significant bleeding occurs despite careful adjustment of the dosage of

warfarin, PST may be an acceptable alternate method of thromboembolism prophylaxis.

CT Check Tags: Comparative Study; Female; Human; Male; Support, Non-U.S.
 Gov't
 Adult
 *Aspirin: TU, therapeutic use
 Clinical Trials
 *Dipyridamole: TU, therapeutic use
 Drug Combinations
 *Heart Valve Prostheses
 Middle Age
 *Pentoxifylline: TU, therapeutic use
 Postoperative Complications: DT, drug therapy
 *Postoperative Complications: PC, prevention & control
 Prospective Studies
 Random Allocation
 *Theobromine: AA, analogs & derivatives
 Thromboembolism: DT, drug therapy
 *Thromboembolism: PC, prevention & control
 *Warfarin: TU, therapeutic use

RN 50-78-2 (Aspirin); 58-32-2 (Dipyridamole); 6493-05-6
 (Pentoxifylline); 81-81-2 (Warfarin); 83-67-0 (Theobromine)

CN 0 (Drug Combinations)

L110 ANSWER 5 OF 7 MEDLINE
 AN 85133261 MEDLINE
 DN 85133261 PubMed ID: 6098626
 TI Study of antiosteoporotic agents in tissue culture.
 AU Robin J C; Ambrus J L
 SO JOURNAL OF MEDICINE, (1984) 15 (4) 319-22.
 Journal code: 7505566. ISSN: 0025-7850.
 CY United States
 DT Journal; Article; (JOURNAL ARTICLE)
 LA English
 FS Priority Journals
 EM 198504
 ED Entered STN: 19900320
 Last Updated on STN: 19900320
 Entered Medline: 19850419
 AB Cultures of osteoblast-like cells were established from calvariae of Sprague-Dawley rats. Pentoxifylline increased cAMP levels and calcium uptake in these cultures. However, calcium uptake increased at lower levels than required to increase cAMP levels. Thus, it is likely that cAMP unrelated mechanisms are also involved in these phenomena.

CT Check Tags: Animal
 Calcium: ME, metabolism
 Cells, Cultured
 Cyclic AMP: ME, metabolism
 Drug Evaluation, Preclinical
 Osteoblasts: ME, metabolism
 *Osteoporosis: DT, drug therapy
 *Pentoxifylline: PD, pharmacology
 Pentoxifylline: TU, therapeutic use
 Rats
 Rats, Inbred Strains
 *Theobromine: AA, analogs & derivatives

RN 60-92-4 (Cyclic AMP); 6493-05-6 (Pentoxifylline); 7440-70-2
 (Calcium); 83-67-0 (Theobromine)

L110 ANSWER 6 OF 7 MEDLINE
 AN 83293098 MEDLINE
 DN 83293098 PubMed ID: 6310016
 TI Studies on osteoporoses. XI. Effects of a methylxanthine derivative. A

AU preliminary report.
 AU Robin J C; Ambrus J L
 SO JOURNAL OF MEDICINE, (1983) 14 (2) 137-45.
 Journal code: 7505566. ISSN: 0025-7850.
 CY United States
 DT Journal; Article; (JOURNAL ARTICLE)
 LA English
 FS Priority Journals
 EM 198310
 ED Entered STN: 19900319
 Last Updated on STN: 19900319
 Entered Medline: 19831021
 AB Heparin (500 U/kg s.c. B.I.D.) induced significant osteoporosis in C3H/St(Ha) female mice after 3 months of treatment. **Pentoxifylline** (12 mg/kg i.m. B.I.D.) prevented this experimental osteoporosis. Osteoporosis was measured by in vivo neutron activation analysis and results were confirmed by atomic absorption spectroscopy. **Pentoxifylline** (0.1-100 microgram/ml) increased calcium uptake and cAMP production in osteoblast-like bone cells isolated from fetal Sprague-Dawley rats. Theoretical implications for osteoblast control of bone resorption are discussed.
 CT Check Tags: Animal; Female
 Bone Resorption
 Calcium: ME, metabolism
 Cyclic AMP: ME, metabolism
 Heparin
 Mice
 Mice, Inbred C3H
 Neutron Activation Analysis
 Osteoblasts: DE, drug effects
 Osteoblasts: ME, metabolism
 Osteoporosis: CI, chemically induced
 *Osteoporosis: PC, prevention & control
 ***Pentoxifylline**: TU, therapeutic use
 Rats
 Rats, Inbred Strains
 Spectrophotometry, Atomic Absorption
 Stimulation, Chemical
 *Theobromine: AA, analogs & derivatives
 RN 60-92-4 (Cyclic AMP); 6493-05-6 (**Pentoxifylline**); 7440-70-2
 (Calcium); 83-67-0 (Theobromine); 9005-49-6 (Heparin)
 L110 ANSWER 7 OF 7 MEDLINE
 AN 82107554 MEDLINE
 DN 82107554 PubMed ID: 6948393
 TI Effect of **pentoxifylline** on red cell flexibility in arterio-sclerotic patients and in patients with heart valve prosthesis.
 AU Johnsson R; Harjola P T; Siltanen P
 SO SCANDINAVIAN JOURNAL OF CLINICAL AND LABORATORY INVESTIGATION. SUPPLEMENT, (1981) 156 297-300.
 Journal code: 2984789R. ISSN: 0085-591X.
 CY Norway
 DT Journal; Article; (JOURNAL ARTICLE)
 LA English
 FS Priority Journals
 EM 198203
 ED Entered STN: 19900317
 Last Updated on STN: 19900317
 Entered Medline: 19820313
 AB Red cell flexibility (RCF) was studied in 40 patients with severe occlusive arterio-sclerotic disease of the lower extremities (Group I) and in 17 patients with aortic or mitral valve prosthesis (Group II). RCF was studied in terms of rigidity and fragility using a filtration method.

Pentoxifylline, which according to our previous observations increases the flexibility of red cells in healthy subjects, also markedly improved RCF in Group I, particularly in terms of fragility. The **pentoxifylline**-induced increase in RCF was less marked in Group II; only the rigidity parameter was significantly decreased. Reid et al [11] reported decreased deformability of red cells in patients with intermittent claudication. Since then a few other studies have been published, in which decreased red cell flexibility (RCF) was observed in patients with diabetic vascular disease [1, 4, 9, 12] and cerebral arteriosclerosis [10]. The objective of this study was to compare RCF in patients with widespread arteriosclerosis and heart valve prosthesis, the latter condition inducing a 'pure' mechanical red cell injury. Both patient groups were also studied after the administration of **pentoxifylline**, a drug known to improve the flexibility of normal red cells--see [6].

CT Check Tags: Female; Human; Male

Adult

Aortic Valve

*Arteriosclerosis: BL, blood

Arteriosclerosis: DT, drug therapy

*Erythrocyte Membrane: DE, drug effects

*Erythrocytes: DE, drug effects

*Heart Valve Prosthesis

Hemoglobins

Middle Age

Mitral Valve

*Pentoxifylline: PD, pharmacology

Pentoxifylline: TU, therapeutic use

*Theobromine: AA, analogs & derivatives

RN 6493-05-6 (**Pentoxifylline**); 83-67-0 (Theobromine)

CN 0 (Hemoglobins)

=> d his

(FILE 'HOME' ENTERED AT 14:51:46 ON 05 AUG 2002)
SET COST OFF

FILE 'REGISTRY' ENTERED AT 14:51:57 ON 05 AUG 2002

L1	1 S PROTEASOME/CN
L2	1 S CHYMOTRYPSIN/CN
L3	5 S 6493-05-6 OR 133343-34-7 OR 134381-21-8 OR 158442-41-2 OR 179
L4	1 S NLVS/CN
L5	3 S C28H43IN4O8S/MF AND 46.150.18/RID AND 1/NR
L6	41 S C32H50N4O8/MF
L7	13 S L6 AND 4/SQL
L8	3 S C28H50N4O7/MF AND OC2/ES
L9	2 S L8 NOT T/ELS
L10	6 S C15H24N2O7S/MF AND NC4/ES
L11	5 S L10 NOT GLYCINE
L12	3 S L11 NOT T/ELS
L13	1 S C19H25BN4O4/MF AND NC2NC2/ES
L14	1 S L3 AND L7
L15	2 S L5 NOT 125I
L16	10 S L3, L4, L9, L12, L13, L14, L15
L17	28 S C34H48N4O5/MF
L18	2 S L17 AND OC2/ES
L19	12 S L16, L18
L20,	STR
L21	1 S L20 CSS
L22	2 S L20
L23	27 S L20 FUL
	SAV L23 GITOMER695/A

L24 15 S L20 CSS FUL SUB=L23
 SAV L24 GITOMER695A/A
 L25 12 S L23 NOT L24
 L26 8 S L25 NOT (C5-C6-C6 OR NCNC2-SC4)/ES
 L27 6 S L26 NOT (T OR SI)/ELS
 L28 16 S L19, L27

FILE 'HCAPLUS' ENTERED AT 15:15:12 ON 05 AUG 2002

L29 2069 S L28
 L30 1598 S L29 AND (PY<=1998 OR PRY<=1998 OR AY<=1998)
 L31 73 S L30 AND L1
 L32 8 S L30 AND L2
 E BONE/CT
 E E3+ALL
 L33 72376 S E8+NT
 E E56+ALL
 L34 3731 S E4+NT
 L35 314 S E8+NT
 L36 2882 S E9+NT
 L37 2828 S E10+NT
 E BONE/CT
 E E3+ALL
 E E58+ALL
 L38 52158 S E3+NT
 E OSTEOPOROSIS/CT
 E E3+ALL
 L39 7181 S E6+NT
 E HYPERPARATHYROIDISM/CT
 E E3+ALL
 L40 1544 S E2
 L41 988 S METAST?(L)BONE(L) (DISEASE OR DISORDER)
 L42 1026 S BONE, DISEASE/CT (L) FRACTURE
 L43 803 S BONE, NEOPLASM/CT (L) METAST?
 L44 141 S OSTEOLYT?(L)BONE(L) (DISEASE OR DISORDER)
 L45 2637 S BONE(L) (SURGERY OR SURGICAL OR POSTPLASTIC OR POST PLASTIC)
 L46 29 S L30 AND L33-L45
 L47 2 S L31, L32 AND L46
 L48 3 S PROSTH?/CW AND L30
 L49 1 S ISOPRENOID AND L30
 L50 4 S L47-L49
 L51 31 S L46, L50
 L52 2 S L30 AND (MUNDY G? OR GARRETT I? OR ROSSINI G?) /AU
 L53 2 S OSTEOSCREEN?/PA, CS AND L30
 L54 32 S L51-L53
 L55 30 S L54 AND (1 OR 63) /SC, SX
 L56 2 S L54 NOT L55
 L57 22 S L55 AND (BONE OR OSTEOP? OR JOINT OR CARTILAG? OR SKELET? OR H
 L58 18 S L55 AND (FRACTURE OR PROSTHE? OR ?NEOPLAS? OR ?TUMOR? OR ?MET
 L59 28 S L57, L58
 L60 2 S L55 NOT L59
 L61 1 S L60 NOT DEXAMETHASONE
 L62 29 S L59, L61
 L63 25 S L62 AND (1 OR 63) /SC
 L64 4 S L62 NOT L63
 SEL HIT RN L63

FILE 'REGISTRY' ENTERED AT 15:29:28 ON 05 AUG 2002

L65 4 S E1-E4
 L66 18 S L1, L2, L28, L65

FILE 'REGISTRY' ENTERED AT 15:30:06 ON 05 AUG 2002

FILE 'HCAPLUS' ENTERED AT 15:30:40 ON 05 AUG 2002

FILE 'BIOSIS' ENTERED AT 15:31:31 ON 05 AUG 2002

L67 3190 S L28
 L68 11694 S EPOXOMICIN# OR EPOXOMYCIN# OR PS341 OR PS 341 OR NLVS OR PSI
 L69 2936 S PENTOXIFYLLIN?
 L70 14427 S L67-L69
 L71 170 S L70 AND 18006/CC
 L72 363 S L70 AND 1800#/CC
 L73 112 S L70 AND 22012/CC
 L74 64 S L73 AND L71,L72
 L75 11424 S L70 AND PY<=1998
 L76 290 S L75 AND L71,L72
 L77 82 S L75 AND L73
 L78 57 S L74 AND L77
 L79 52 S *1800#/CC AND L78
 L80 50 S *22012/CC AND L78
 L81 53 S L79,L80
 L82 9 S L81 AND (BONE RESORPTION OR ANTIOSTEOPOR?)
 SEL DN AN 2 6 7
 L83 3 S L82 AND E5-E10
 L84 4 S L70 AND (MUNDY G? OR GARRETT I? OR ROSSINI G? OR GARRETT R?) /
 L85 0 S L70 AND OSTEOSCREEN?/CS

FILE 'BIOSIS' ENTERED AT 15:43:20 ON 05 AUG 2002

FILE 'MEDLINE' ENTERED AT 15:43:28 ON 05 AUG 2002

L86 11161 S L70
 E BONE AND BONES/CT
 L87 102 S E3+NT AND L86
 E BONE DISEASE/CT
 L88 58 S E8+NT AND L86
 E HYPERPARATHYROIDISM/CT
 L89 129 S E3+NT AND L86
 E OSTEOPOROSIS/CT
 L90 9 S E3+NT AND L86
 E FRACTURE/CT
 L91 11 S E106+NT AND L86
 L92 1 S (E4+NT OR E59+NT) AND L86
 L93 2 S (MUNDY G? OR GARRETT I? OR ROSSINI G? OR GARRETT R?) /AU AND L
 L94 177 S L87-L92 AND PY<=1998
 L95 3 S L94 NOT AB/FA
 E PROSTH/CT
 L96 67 S E7+NT AND L86
 L97 52 S L96 AND PY<=1998
 L98 220 S L94,L97
 E BONE DEMINERALIZATION/CT
 L99 0 S E11+NT AND L86
 L100 17 S E33+NT AND L86
 L101 22 S E40+NT AND L86
 E BONE MINERALIZATION/CT
 E E3+ALL
 L102 4 S E2+NT AND L86
 E BONE REMINERALIZATION/CT
 E E2+ALL
 L103 1 S E2+NT AND L86
 L104 25 S L100-L103 AND PY<=1998
 L105 6 S L98,L104 NOT AB/FA
 L106 218 S L98,L104 NOT L105
 L107 206 S PRIORITY JOURNALS/FS AND L106
 L108 180 S ENGLISH/LA AND L106
 L109 171 S L107 AND L108
 L110 7 S L28 AND L109
 SEL DN AN 5 6

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L111 164 S L109 NOT L110

FILE 'MEDLINE' ENTERED AT 15:55:16 ON 05 AUG 2002